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**W. B. SAUNDERS COMPANY, Philadelphia and London**

VOLUME 24 *Cleveland Clinic Number* NUMBER 2

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THE  
MEDICAL CLINICS  
OF  
NORTH AMERICA

*MARCH, 1940*

PHILADELPHIA AND LONDON

W. B. SAUNDERS COMPANY

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PUBLISHED BI-MONTHLY (SIX NUMBERS A YEAR), BY W. B. SAUNDERS COMPANY, WEST WASHINGTON  
SQUARE, PHILADELPHIA.

MADE IN U. S. A.



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Cleveland Clinic Number  
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Volume 24

March, 1940

Number 2

**HEADACHES OF ALLERGIC ORIGIN**

J. WARRICK THOMAS AND C. R. K. JOHNSTON

**Historical.**—The rapid advances made in the study of allergy during the past two decades have focused attention on the problem of *migraine*. However, there seems little doubt that "sick headache" has been known for many centuries and its association at times with the prior ingestion of certain foods was probably often recognized long before the allergic nature of such headaches was established.

Vaughan, Tuft and others have considered the historical background in some detail and generally credit Aretaeus, during the first century, with differentiating this type of headache from others, and calling it "heterocrania." Galen was probably the first to speak of hemicrania in describing this symptom-complex. He attempted to explain it on the basis of a cortical irritation by "black bile."

Little progress was made in establishing the allergic etiology until early in the present century, although many French authors had suggested the allergic basis during the nineteenth century. Rowe and Vaughan give credit to Lesne and Richet, Jr. (1913) for the first definite suggestion that migraine might be caused by allergy to egg or milk. Pagniez and associates, Lubbers, and many others quickly added to the evidence. Vaughan is generally credited as being the first in this country to demonstrate conclusively the allergic etiology of migraine by obtaining relief of symptoms following the avoidance of foods by patients reacting positively to skin tests and the sub-

sequent production of symptoms by feeding the suspected foods.

**Definition.**—The word “migraine” is derived from the Greek term “hemicrania” and denotes a periodic, or recurrent, type of headache, often quite incapacitating, usually unilateral, and frequently preceded or accompanied by an “aura,” usually visual in type, and as a rule terminating in nausea and/or vomiting. “Sick headache” is the term usually applied by the laity.

All degrees and variations of the above description may exist, from the severe blinding or splitting headache to very mild forms. Some authors stress various types of migraine according to the predominating symptom, such as the ocular, menstrual, or bilious type. Frequently one or more symptoms are absent and headache may occur alone. At times certain visual or cerebral manifestations may exist without headache, and these have been referred to as “migraine equivalents.”

The definition of migraine may be misleading in that one is prone to recognize the typical, severe, paroxysmal headache but may overlook the *mild type* with vague gastro-intestinal distress. Migraine should be suspected in all types of *atypical* headaches of periodic nature *when no other definite cause is evident*. This is especially true if the headache is accompanied by *gastro-intestinal symptoms*.

**Pathology.**—The pathology of migraine is as yet unknown. However, an allergic basis for the attacks seems quite plausible in view of the recent report by Cobb of vasomotor control of the cerebral arteries, since localized edema can now be explained on the basis of capillary vasodilatation and increased permeability. Rowe<sup>1</sup> explains the symptoms as an allergic phenomenon, either due to a localized edema of the meninges or possibly of the brain parenchyma, or else as being due to vascular spasm arising from smooth muscle contraction as a result of localized areas of allergy in the blood vessels. He quotes numerous authors in support of one or other of these views. Many favor the view of impairment in liver function, which may be caused by a localized allergic

reaction in the liver. Rowe suggests that the liver is one of the "shock" organs in man.

Goltman<sup>2</sup> has recently reported a case of typical migraine in a patient with a family history positive for allergic disease who was operated upon for supposed brain tumor. Cranio-cerebral operation was performed while the patient was suffering from a severe headache. The dura was found to be tight, the blood vessels dilated, and the brain was wet. A quantity of fluid escaped under increased pressure when the dura was opened. Following the operation, the trephined area was observed during the occurrence of headaches. Before the onset of pain, the face was pale and the opening in the skull depressed. As the headache progressed, the depression began to swell and finally bulged and felt tense. Later, as vomiting occurred, the face became flushed, and after cessation of the attack, the swelling in the operative site gradually receded. The ingestion of wheat would consistently produce a typical attack. On skin testing, wheat gave a positive reaction and the patient was relieved of symptoms by allergic therapy.

Goltman interprets the mechanism of the attack as an initial vasomotor spasm, evidenced by the blanching of the face. Secondary vascular dilatation then occurs, with resulting edema of the brain and, in this case, by bulging of the trephined area. He believes the pain is due to swelling of the brain which probably produces a temporary disproportion between the size of the cranial cavity and the brain. Finally, there is a temporary hypersecretion of cerebrospinal fluid, followed quickly by hyperabsorption which tends to equalize the pressure within the subarachnoid space.

This case of Goltman's lends considerable support to the allergic basis of the attacks and suggests a close similarity with other allergic lesions.

**Classification.**—The question of classification of the allergic or migraine-type of headache is not one to be considered lightly. It is very difficult to think of headaches as a general subject as they are often found to be only a symptom of some other disease entity.

For purposes of simplicity we will outline headaches under two general headings, both of which will be further subdivided. We may classify headaches, from the point of view of allergy, under the headings of (1) *allergic headaches*, and (2) *non-allergic headaches*.

*Allergic Headaches*.—The allergic or true migraine headache is usually that type of headache which comes on *intermittently* and is of a *severe* type; it has to be distinguished from headaches due to other causes. It is usually found to follow the exposure to certain *allergens*, whether they be *foods* or *ingestants* or *inhalants*, etc.

These headaches are usually incapacitating and may be *unilateral*, generally involving one or the other side of the head in the beginning; later they become generalized. They may be accompanied or preceded by *cortical* or *sensory disturbances* of visceral type, and are later found to end in *nausea* or *vomiting*. Rowe,<sup>1</sup> for purposes of better understanding, divided the types of migraine into four stages: the *prodromal period*, the *period of auras*, the *attack*, and the *post-migrainous stage*.

Vaughan and Todd, in going over the literature, both have summarized the *symptoms* of migraine: There may be premonitory hyperactivity, irritability, and depression with eye symptoms of disturbed or blurred vision, as well as emotional unbalance, yawning, insomnia, profound sleep, fatigue, bad breath, canker sores, abnormal appetite, nausea, vomiting, constipation, indigestion, body aching, stretching, or chilliness. The attack may progress, with more pronounced visceral and vasomotor symptoms and with involvement of the cranial or peripheral nerves. The pain is variable in intensity and location and may be progressive in that certain areas are involved in succession. The gastro-intestinal symptoms of nausea and vomiting involve all ages and are variable in duration from a few minutes to several hours and are variable in severity. A single attack may persist from a few hours to several days or a week. The *residual symptoms* or post-migrainous symptoms may be characterized by general malaise to varying degrees of exhaustion, drowsiness, anorexia, polyuria, and rhinorrhea. At

times, along with migraine there may be other conditions, such as transient psychosis, ocular palsies, neuralgia, paroxysmal tachycardia, and epilepsy—all of which have been described by various authors.

We have to think of headaches that are secondary to nasal obstruction, or the "*sinus headache*," as one that may be thought to result from nasal or upper respiratory allergy. Frequently, patients will complain of headaches secondary to nasal obstruction which may be unilateral. These headaches are not characteristic in type as compared with the typical migraine or allergic headache and they lack such symptomatology. The periodicity of the characteristic migraine is found to be absent.

*Nonallergic Headaches.*—Among the nonallergic headaches, we will only attempt to group them under the general headings which will serve as a partial outline to contrast them with the allergic or migraine type of headache. We shall not go into a detailed discussion as space does not permit.

The following is a brief outline of some of the more important types and causes of nonallergic headache:

1. Headaches secondary to *eye strain* or other eye conditions.
2. *Neurologic* headaches.
3. *Endocrine* or *metabolic* headaches.
4. *Gastro-intestinal* headaches.
5. Headaches associated with *cardiovascular* disease.
6. Headaches related to or resulting from *bacterial infections*, including headache of *syphilitic* origin.
7. Headaches associated with *arthritis*.
8. *Psychogenic* headaches.
9. *Miscellaneous* headaches, or headaches of undetermined origin.

This grouping is made with no other idea in mind than considering a few of the possible etiologic factors relative to the nonallergic group of headaches.

The question of *differential diagnosis* of migraine has to be considered by the nature of the allergic etiologic factors, including other manifestations of allergy which might be asso-

ciated in addition to the migraine or presenting problem. In many instances the presence of migraine may be questionable; or a true migraine may be present associated with other conditions. We have to remember that each patient presents a different problem and should be studied as such. Where there is some other condition to be considered, the part of such a factor has to be either proved or disproved as being related to the existence of the headache.

After considering the *detailed history*, we outline a program of investigation which may include any of the *routine* or *special laboratory studies*, such as roentgen examination, determination of the basal metabolic rate, along with sensitization studies for the various foods, inhalants, bacteria, molds, pollens, etc., depending on the individual case. The type and the extensiveness of the *sensitization studies* depends on the presence of other allergic manifestations. In investigating and studying the patient with allergy, we endeavor to try to control it as far as possible for various allergic manifestations, as they are all interrelated. It is our purpose to *lessen the allergic overload*, as this is a most important factor in any and all of the allergic manifestations.

When the patient has problems that are questionable, and dealing with other branches of medicine, they are referred to specialists in those fields, for example, endocrinology, otolaryngology, or neurosurgery. We have to evaluate the recommendations resulting from such consultations, weighing carefully the opinions presented and finally *correlating all the data* that are present before placing the patient on a program of treatment.

**Illustrative Cases.**—We will present several cases of migraine for purposes of illustrating the type of history along with the findings in the individual cases, including the treatment and the progress of the patient:

*Case I.*—This patient, a white woman thirty-three years of age, came in with a chief complain of headaches since the age of six. At the time of onset, these headaches were right-sided.

Six months prior to admission, symptoms had become progressively worse. There were no visual disturbances; however, nausea and vomiting accompanied the headaches. The headaches were more severe at the time of the menstrual period. There was a definite history of pork causing an exacerbation of the headaches. She had had recurrent hives until the age of six. There was a family history of her mother having had migraine. At times the headaches had been less severe than at other times.

Physical examination revealed upper and lower dental plates. There was nothing else of clinical significance found on physical examination. The patient had a complete allergy survey and gave positive reactions to a number of the foods to which she was tested. She was then placed on a program of dietary restrictions and told to maintain an avoidance regimen for two months, after which time her program would be further modified. She gave several positive reactions to the inhalants to which she was tested and so was instructed to avoid them. Positive bacterial reactions were encountered following sensitization studies with the stock bacteria which were not included in her original program of treatment. The patient was instructed to keep a food diary on furnished forms.

This patient was first observed six weeks after her initial study, and at that time she reported that she was much improved and that her headaches had been fewer. She also stated that she had found from her own experience that cinnamon, lettuce, and chocolate all caused her trouble, so these were then eliminated. She continued to get along satisfactorily for approximately two months, and reported that she had some recurrence of her headaches after trying to broaden her diet. She had been suffering from some gastro-intestinal symptoms simulating gallbladder disease. A gastro-intestinal series failed to reveal anything of significance; however, films of the gallbladder revealed several nonopaque calculi. We made up an enteropathogen vaccine and, after receiving a series of injections, the patient showed some further improvement of symptoms. The basal metabolic rate at this time was found to be —14. She responded somewhat to thyroid extract.

Taking this patient's progress into consideration, we feel that she observed some 75 per cent improvement in her headaches and that she was able definitely to incriminate certain foods that caused her trouble.

*Case II.*—A white woman, twenty-three years of age, complained of severe headaches since early childhood. They were infrequent at the time of onset, occurring one to three times each year; they then became more frequent and severe up until the age of twelve years, at which time they became almost continuous for a period of two months. During this time the patient was practically incapacitated. She showed some improvement after this period and again experienced headaches on an average of one every three months up until one year prior to her present examination. From then on her headaches averaged one every seven to ten days. They were hemicranial in distribution, more often involving the right side, and at times were generalized. Their average duration was about twenty-four hours. The onset of the headaches was not limited to any special time of the day, but they were associated with nausea and vomiting. The patient had an excessive appetite and a moderate euphoria on the day before onset. She stated that she had two kinds of headaches: the severe kind, as described above, and a mild type which at times was readily relieved by aspirin. She received some ovarian extract with no improvement.

During the twelve months prior to admission, she had rather marked gastro-intestinal symptoms consisting of epigastric burning, coming on two or three hours after meals. Eating gave definite relief. When working under extreme nervous tension, she felt that her gastro-intestinal symptoms were worse. There was some associated nausea and vomiting even in the absence of headaches. The severe nervous symptoms subsided after she discontinued her work as a telephone operator. Her history included nasal obstruction with an associated rhinorrhea and an increased frequency of sneezing. She had a submucous resection some eighteen months prior to admission

and since that time her symptoms have been more pronounced on the right side. Exposure to cold and upper respiratory infections aggravated the nasal symptoms. There was a family history of her mother having had asthma and sick headaches. A paternal grandmother also had migraine. Physical examination revealed nothing of clinical significance.

Sensitization studies revealed positive reactions to a number of the foods, the more important of which were potatoes, pineapple, coffee, milk, olives, and chocolate. She gave positive reactions to a number of the common inhalants and molds and was placed on a program of hyposensitization. She was observed at six-week intervals, at which times her diet was modified. During such intervals she kept an accurate food diary. We were able to incriminate certain foods as causing her trouble, these foods were eliminated from her diet, with definite improvement of symptoms immediately after dietary restrictions were instituted. She gradually observed improvement of the nasal symptoms on a program of hyposensitization.

Nine months after the initial studies, the patient reported that she was getting along nicely and had only an occasional headache due to some definite dietary indiscretion which she herself could recognize.

*Case III.*—This patient, a white woman some thirty-nine years of age, was referred to us for study by the Department of Endocrinology. She complained of headaches, nervousness, and gastro-intestinal symptoms characterized by epigastric pain, weakness, etc. There was a history of intermittent nasal obstruction since November, 1938, with associated mucoid secretion and some postnasal drip. There were no inhalant or ingestant aggravating factors. There was a history of a chronic cough for the past two years which had persisted up until the present time. Symptoms were definitely worse at night. In the beginning, there was some substernal tightness and labored wheezing respiration at the onset of her cough. During the past two years she complained of sick headaches which were frontal or generalized in their distribution, and associated with

nausea and vomiting of from twenty-four to thirty-six hours' duration. These headaches were more pronounced prior to catamenia. There was a definite history of cabbage, cauliflower, apples, and pork causing gastro-intestinal upset. The family history revealed several brothers with chronic catarrh.

On physical examination the patient was found to be slightly obese. The chest examination revealed a few typical asthmatic râles, especially in the right chest anteriorly. The nasal mucous membranes were pale, boggy, and congested. There was a midline lower abdominal incision resulting from bisalpingo-oöphorectomy three years previously. The balance of the physical examination revealed nothing of significance.

The patient was studied by the Department of Endocrinology and was found to have hypo-ovarianism. A complete allergy survey was made and she gave significant reactions to a number of foods, mainly eggs, corn, rice, coffee, members of the cabbage family, spinach, citrus fruits, lettuce, and artichoke. Among the common inhalants and molds she gave strong reactions to mattress dust and tobacco smoke and ashes. She was placed on a program of dietary restriction, eliminating the foods to which she was found allergic, and she was instructed to avoid tobacco smoke as well as the other inhalants to which she reacted. In addition, we instituted a program of hyposensitization with the inhalants and molds. This patient kept a food diary which enabled us to detect certain of the foods which were not formerly suspected of causing her trouble. She responded favorably to treatment and was dismissed from active observation at the end of eight months, at which time she was symptom-free.

The main point of interest in this case is that of a combined *endocrine problem* along with migraine and a *perennial allergic rhinitis*, all three of which had to be adequately controlled before the patient was symptom-free.

*Case IV.*—A white man, some thirty-five years of age, gave a history of having had migraine, hay fever, and perennial allergic rhinitis for the past eleven years. He was able definitely

to incriminate both cats and dogs, as well as dust and several of the pollens. He was a physician by profession and found it difficult to carry on his work owing to contact with the various inhalant factors when making certain house calls. He knew from his own experience that certain foods caused severe incapacitating headaches, with associated gastro-intestinal symptoms characterized by heartburn and regurgitation. In early childhood he had had hives on two occasions. His headaches were variable in occurrence, averaging one every three weeks to three months, depending on how closely he adhered to his diet.

Sensitization studies were made and he was placed on a program of dietary restrictions, eliminating those foods to which he gave positive reactions by skin test and, in addition, certain foods that he himself knew, from his own experience, caused him trouble. He was given preseasonal ragweed and grass hyposensitization injections along with an inhalant extract. We were able to control the nasal symptoms quite satisfactorily during the winter months and to a large extent during the pollen season. He was able to control his headaches entirely after instituting the program of dietary restrictions. He has experienced recurrent headaches, however, since that time following dietary indiscretions. He stated, however, that he had occasionally been able to take foods that he knew had caused him trouble at odd intervals, but that repeated exposure to such foods usually resulted in a typical attack of migraine. For the control of symptoms he found it necessary to take several opiates and atropine along with nembutal. These drugs, however, did not always give him relief. The duration of the headaches averaged from six to some thirty-six hours.

This case is illustrative of a definite migraine associated with other frank manifestations of allergy which can be controlled satisfactorily.

*Case V.*—This patient, a married woman of forty-four, came to the Clinic in April, 1936, complaining of migraine which had been present since the age of five. The headaches

were always generalized, beginning in the occiput. No scotomata were noted, but nausea and vomiting occurred until about the age of twenty-five; since then only nausea was present. The headaches recurred only once every month or two, and lasted from twelve to twenty-four hours, but they were severe and were becoming more so. There was no relation to the menses, which were regular. She incriminated no foods, but felt worry and nervousness were aggravating factors. She also had a chronic anterior and posterior nasal mucoid discharge, but no other present or past history of allergy. Her mother had hay fever and migraine, while her maternal grandfather and one aunt also had had migraine.

Physical examination revealed two devitalized teeth and a systolic blood pressure of 170 and diastolic of 120. A special ophthalmologic examination revealed a low-grade edema of the optic discs and some arterial changes consistent with a diagnosis of early malignant hypertension.

Routine laboratory examinations were entirely negative with the exception of a trace of albumin in the urine. The basal metabolic rate was  $-4$  per cent.

Allergy tests revealed sensitivity to feathers, house dust and a large number of foods, including milk, wheat, pork, potato, beans, shell-fish, and several fruits and vegetables. The patient was advised to avoid carefully the inhalant and food allergens, but was given no hyposensitization therapy.

Two and a half months after beginning the regimen, her doctor wrote to say she had been free of symptoms and felt better than at any time in her life. She was seen in February, 1939, thirty-four months after her original visit and reported only one severe headache and two milder ones during that period. They were still typical in that they were the same type of generalized headache, with nausea. The nasal allergy had shown little or no improvement, though she had covered her pillow with an allergen-proof encasing and was avoiding the other inhalants as far as possible. She had no other complaints at this time and her blood pressure was now 178 systolic and 108 diastolic. Her menstrual periods were still regular and no menopausal signs had appeared.

*Case VI.*—The patient, a man aged thirty-nine, came to the Clinic on June 17, 1938, complaining of "sick headaches" for three years. They had begun insidiously, but had gradually become more marked and more frequent, recurring as often as every two weeks when he was first observed. A visual aura, with inequality of the pupils, preceded an attack. The headache was always bilateral, and terminated in five to six hours after nausea and vomiting occurred. The patient believed that overwork and nervous strain would precipitate an attack, but could incriminate no food, though eggs were suspected. The attacks were more frequent over the weekend. No other allergy was present except a chronic, mucoid postnasal drip, at all seasons.

The patient's father had a perennial rhinitis, and his great grandfather and two great uncles had had migraine.

The general physical examination was entirely negative except for large, pale turbinates, which were interpreted by the Nose and Throat Department also as typical of allergic rhinitis. Routine urinalysis was negative and the blood counts showed only a 3 per cent eosinophilia. Allergy studies revealed sensitivity to dust and tobacco, as well as several foods, notably the entire pea-bean group, wheat, rice, corn, shell-fish, nuts, turkey, and several fruits and vegetables. Beans were the strongest reactors, varying from 1 plus to 3 plus sensitivity.

A careful dietary regimen, eliminating all the positive foods, was advised as well as avoidance of the inhalants insofar as possible. No hyposensitization was carried out, but the patient was given thyroid.

The patient returned in a little over four months and reported that he felt fine and had had only one headache which followed a break in his diet (wheat and turkey). The nasal symptoms were also improved (at least 50 per cent), though he had not been able to avoid the inhalant allergens well. In retrospect, he felt that beans had been the chief cause of his trouble, as about 90 per cent of his headaches occurred on Sundays and he had eaten beans nearly every Saturday.

Seven months later we again learned that he was still doing fine and had had no further headaches.

## TREATMENT

The question of treatment of migraine is very varied and in some instances extensive. These patients are usually willing to submit to anything in order to gain relief. The following outline will serve as a partial guide to be considered in the management of these individuals.

**Symptomatic.—**

- (A) 1. Ergotamine tartrate (gynergen 0.25 mg.) (hypodermic most effective).
2. Epinephrine 1:1000 (adrenalin, minims 5–15).
3. Coal tar derivatives (acetanilid, phenacetin, or aspirin).
4. Barbituric acid derivatives (sodium amytal, phenobarbital, nembutal, etc.).
5. Endocrine therapy, including pituitrin.
6. Saline cathartics and colonic irrigations.
7. Gastric lavage.
8. Avoidance of fatigue and emotional upset.
9. Cold applications, and in some instances heat.
10. Narcotics (codeine, morphine, dilaudid, etc.).
11. Oxygen by inhalation.

**Therapeutic or Curative.—***(A) History:*

1. Elimination of known offenders.
2. Elimination of suspected offenders.
3. Elimination of dietary offenders.
4. Keeping of food diary.

*(B) Other allergic management and therapy:*

1. Avoidance of and hyposensitization to inhalant factors (common inhalants, molds, and pollens).
2. Autogenous vaccine and nonspecific therapy.

*(C) Digestive aids:*

1. Diluted hydrochloric acid.
2. Bile salts.
3. Pancreatic enzymes.

(D) *Surgical treatment:*

1. Removal of foci (teeth, gallbladder, tonsils, etc.).
2. Sympathetic ganglionectomy.

(E) *General measures:*

1. Control of nervous factors along with adequate rest. Maintenance of adequate diet and vitamin intake.
2. Use of certain glandular products, as indicated.

### SUMMARY

1. Migraine is discussed from the point of view of historical background, definition, and pathology.

2. Headaches are classified as allergic and nonallergic headaches. The allergic headache is discussed regarding etiology and symptomatology. The nonallergic headaches are grouped for the purposes of classification and to distinguish them from the allergic type. They are considered from the point of etiology or associated clinical manifestations.

3. Case reports of the allergic or migraine headaches illustrate typical histories and the occurrence of migraine *per se* as well as with other allergic manifestations. Sensitization studies are discussed as well as the type of treatment instituted. The results of the treatment are given in each individual case.

4. The treatment is outlined according to the best method as recognized by leading allergists.

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## HEADACHES CAUSED BY INTRACRANIAL LESIONS

A. T. BUNTS

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ALTHOUGH chronic headache is not commonly due to organic intracranial lesions, it is essential to bear in mind the possibility of such etiologic agents during the clinical analysis of any form of headache.

### FUNDAMENTAL CONCEPTS

In order to provide a sound foundation for our understanding and interpretation of headache, it is worth while to consider briefly some of the modern ideas concerning the mechanism of intracranial pain. During the past decade experimental attack upon the problem by a number of workers has yielded important knowledge. Neurosurgeons, while operating under local anesthesia, have found that the brain proper with its pial envelope is insensitive to puncture and to incision. Little or no pain is produced by incision of the dura, except near the base and over the middle meningeal artery when it is clipped and divided. Penfield<sup>1</sup> has found that the venous sinuses of the dura are sensitive to pressure, traction, heat and electrical stimulation. He observed that pain from stimulation of the meningeal arteries is often sharp and well localized. Pain derived from stimulation of the dural sinuses is usually referred to a distance.

The innervation of the intracranial blood vessels and dural sinuses has been thoroughly studied and described by McNaughton.<sup>2</sup> The middle meningeal artery carries a perivascular plexus of sympathetic fibers from the external carotid plexus and receives a rich supply of nerve fibers from the three divisions of the trigeminal nerve, chiefly from its second and third divisions. These nerves supply the dura adjacent to the arte-

rial branches. The anterior end of the superior sagittal sinus is supplied by anterior ethmoidal branches of the first division of the trigeminal nerve and by nerves accompanying the terminal branches of the middle meningeal artery. The nervus tentorii arising from the first division of the fifth nerve supplies the tentorium, the superior walls of the straight and transverse sinuses, the occipital dura, the posterior third of the falx, and the posterior third of the superior sagittal sinus. The meningeal branch of the vagus nerve sometimes supplies the inferior walls of the transverse sinuses, and twigs from the ninth and tenth cranial nerves supply the sigmoid sinus and jugular bulb. The pial and intracerebral arteries also have a plentiful nerve supply, but afferent pathways from these vessels have not been definitely established.

The brilliant clinical investigations of H. G. Wolff<sup>3, 4, 5, 6, 7</sup> and his co-workers have shed much light on the mechanism of headache. They have shown that the headache following intravenous injection of histamine is produced by distention of cranial arteries (temporal, occipital, and middle meningeal arteries). It is their belief that the same mechanism of arterial stretching gives rise to the migraine headache, and that the termination of the histamine headache and the migraine headache by ergotamine tartrate is due to the capacity of this agent to constrict these cranial arteries and thus reduce the amplitude of their pulsations. The same investigators have demonstrated such a mechanism for pain in the headache resulting from fever and in the headache of hypertension. In their studies of afferent nerve pathways, they have presented evidence which strongly suggests that impulses from cranial arteries of the front of the head conducted through the sensory root of the fifth cranial nerve are mainly responsible for frontal, temporal, and parietal headache. Impulses from cranial arteries from the back of the head may be conveyed over the upper cervical sensory roots, giving rise to occipital headache.

Northfield<sup>8</sup> was able to produce headache in man by suddenly increasing or decreasing the intracranial pressure, and after other ingenious experimental studies, he concluded that

the dura is not the sensitive structure responsible for the headaches of intracranial tumor, but that such headaches are caused by an abnormal state of tension in the walls of the cerebral blood vessels.

In the opinion of Pickering,<sup>9</sup> most headaches of intracranial origin are probably due to tension. He believes that the regions where tension may produce pain are around the intracranial arteries (*e. g.*, during dilatation of these vessels), and possibly also around the venous sinuses of the dura (*e. g.*, during displacement of the brain or parts of it).

Elsberg and Southerland<sup>10</sup> thought it probable that the headache occurring during encephalography under local anesthesia might be related to the presence of air in the third and lateral ventricles, with transmission of pressure changes to the thalami in the walls of the ventricles. This theory cannot be entirely dismissed when one considers the not uncommon occurrence of so-called "thalamic pain" following vascular lesions of the internal capsule.

The most convincing evidence to date definitely favors the concept that headache is related to alterations in the *tonus* of intracranial arteries, and of the meningeal arteries in particular. It is also probable that changes in tension of the walls of the intracranial venous sinuses play a part in the production of some headaches. Many and diverse are the factors which may operate to bring such mechanisms into play.

#### CLINICAL CONSIDERATIONS

Intracranial lesions which give rise to headache may be located in the *meninges*, in the *brain*, or in the *blood vessels*. No discussion of the manifestations of syphilis in these structures will be made here, inasmuch as this disease has been given special consideration by Dr. Earl W. Netherton elsewhere in this symposium.

**Diseases of the Meninges.**—The meninges may be the site of *inflammatory lesions* of many varieties. Almost every known pathogenic organism has been found capable of causing meningitis. Any febrile illness associated with listlessness,

nuchal rigidity, and Kernig's sign should suggest the importance of spinal fluid examination. A cellular reaction in the fluid, together with identification of the causative organism in the stained smear or on culture, will establish the diagnosis. The most severe headache ever studied by the writer occurred in a case of extradural abscess which had originated in a long-standing osteomyelitis of the skull and which had gradually stripped the dura away from the inner table of the skull over the left frontal lobe of the brain. The changes in the bone were seen in the roentgenogram, but the abscess was found only by trephine.

*Tumors of the meninges* occur not infrequently; they are usually meningiomas (dural endotheliomas) which arise from the inner layer of the dura or from the arachnoid anywhere within the cranial cavity. By involvement of various functional centers of the brain and the cranial nerves, they give rise to definite neurologic symptoms and signs. When the location and size of a meningioma is such as to cause obstruction of the normal outlet of cerebrospinal fluid from the ventricular system, it will produce papilledema and headache. This mechanism may occur in association with any intracranial tumor.

**Diseases of the Intracranial Blood Vessels.**—Conditions which may cause headache are *thrombosis, embolism, syphilis, arteriosclerosis, hemorrhage, and aneurysm*.

*Spontaneous subarachnoid hemorrhage*, usually the result of rupture of a small aneurysm of the circle of Willis or one of its branches, is characterized by sudden onset of severe headache, collapse, possible stupor or cranial nerve signs, and grossly bloody spinal fluid.

*Chronic subdural hematoma*, a slowly expanding cystic lesion containing old broken-down blood and resulting from the rupture of veins coursing from cortex to dural sinuses during head injury, is usually situated over one or both cerebral hemispheres. Such a lesion may not begin to make itself manifest until several weeks after a minor or major injury to the head, when headache ushers in a train of symptoms and signs characterized by listlessness and mental sluggishness with

the inconstant addition of neurologic signs such as abducens weakness, cortical facial paresis, and weakness of an arm or leg. Papilledema and increased intracranial pressure are by no means present in all cases of subdural hematoma. Encephalography may aid in establishing the diagnosis in some cases, but unilateral or bilateral trephine is the court of last appeal and permits diagnosis and treatment through the same bony opening.

*Aneurysms* within the skull are most frequently located in the intracranial portions of the internal carotid arteries. They may give rise to headaches and unilateral involvement of the oculomotor nerves and the optic nerve, even to the extent of complete ophthalmoplegia and optic atrophy of one eye. Roentgen examination of the skull sometimes reveals a curved line of calcification in the wall of such an aneurysm just lateral to the sella turcica. Arteriovenous communications between the internal carotid artery and the cavernous sinus are usually the result of trauma, and they may give rise to headache, ophthalmoplegia, bruit, thrill, and pulsating exophthalmos. Headache may also be caused by various types of vascular malformations and blood vessel tumors of the brain itself; these lesions, usually located in the cortex, often cause generalized or focal convulsive seizures.

**Diseases of the Brain.**—Diseases of the brain are commonly associated with headache. Inflammatory lesions, such as *encephalitis* and *abscess*, and *tumors* of various types, must be borne in mind during the clinical analysis of this symptom.

*Encephalitis* is most often the result of a filterable virus infection, as in epidemic encephalitis, but may be caused by the toxins of various pathogenic organisms. It has occurred as the result of influenza, chicken-pox, scarlet fever, mumps, and undulant fever. The disease is usually febrile and may be accompanied by somnolence, coma, psychotic manifestations, diplopia, convulsions, or signs of focal involvement of the brain. Intracranial pressure may be increased, with concomitant papilledema. The cerebrospinal fluid may show a moderate increase in cell count, the majority of the cells being lymphocytes.

*Abscess of the brain* occurs most often as the result of bacterial invasion from a neighboring infection in a frontal sinus, mastoid, or middle ear, but it may also develop as the result of septic emboli from a pulmonary abscess. The lesion may be accompanied by fever or not; evidence of focal involvement of the brain is often present, and not uncommonly there is an increase of intracranial pressure and a slight increase in cell count in the cerebrospinal fluid.

*Tumors of the brain* may arise primarily from the cellular elements of that organ, or they may be secondary metastases from neoplasms in other parts of the body. Occurring at any age, they are rarely accompanied by fever and they give rise to a host of varied neurologic symptoms and signs, which often indicate involvement of certain specialized functional areas of the brain. When such tumors are situated so as to cause obstruction to the normal flow of cerebrospinal fluid from the ventricular system, internal hydrocephalus occurs, intracranial pressure is increased, and headache and papilledema are produced. This condition is most common in the presence of tumors of the cerebellum and fourth ventricle, tumors of the pineal body and third ventricle, and tumors involving the basal ganglia. Inflammatory lesions of the aqueduct of Sylvius or of the foramina of Magendie and Luschka in the fourth ventricle may cause internal hydrocephalus, thus simulating tumors. Headache may be absent throughout the entire course of a brain tumor. The location of headache does not necessarily indicate the intracranial site of a neoplasm. Neurologic examination, study of the visual fields and optic fundi, and cerebral pneumography are important aids in the localization of brain tumors.

**Posttraumatic Headache.**—This is one of the commonest and most distressing symptoms which occur after head injuries of any degree of severity, and it may persist for many months or even for years. Its exact etiology is uncertain, but it is thought to be related in some way to gliosis following petechial hemorrhages in the brain, to scar formation following similar hemorrhages in the dura, or to adhesions between the

dura and pia-arachnoid. *Dizziness* and *emotional instability* are common accompaniments of this type of headache. There is usually a paucity of objective signs in these patients. Occasionally in such cases encephalography reveals gross changes in the structure of the brain, such as atrophy of a cerebral hemisphere with enlargement of the ipsilateral ventricle and absence of cortical subarachnoid air markings over one or both cerebral hemispheres. Lumbar air insufflation relieves some of these posttraumatic headaches, but our experience has not been as fortunate as that of Drayton,<sup>11</sup> who reported complete relief of headache in 89 per cent of forty-six patients.

**Lumbar Puncture Headache.**—Lumbar puncture headache fairly often follows removal of cerebrospinal fluid from the lumbar subarachnoid space and may be accompanied by vomiting and stiffness of the neck. It can often be prevented by keeping the patient flat in bed without a pillow for from twenty-four to forty-eight hours after the puncture. This type of headache is considered to be due to leakage of cerebrospinal fluid through the hole or holes in the dura produced by the needle, and it is accompanied by a low cerebrospinal fluid pressure (Merritt and Fremont-Smith<sup>12</sup>). Characteristic of this headache is that it disappears whenever the patient lies down and returns when he assumes the erect position. Rest in bed for two or three days followed by slow and cautious resumption of activities is the most important feature in the treatment of this condition, and during that time the patient should be encouraged to drink plenty of fluids.

#### SCHEME FOR INVESTIGATION

An accurate *history* is of primary importance in the analysis of headache, and it should include information regarding the *quality*, *location*, and *duration* of the pain, as well as its relation to other factors such as *reading*, *fatigue*, *posture*, *menstrual function*, and *gastro-intestinal function*.

If the history suggests an *intracranial cause* for headache, one or more of the following examinations may be necessary to establish the diagnosis:

1. Complete physical and neurologic examinations.
2. Blood counts and smear.
3. Blood Wassermann reaction.
4. Urinalysis.
5. Visual field examinations and ophthalmoscopic examination of the optic fundi.
6. Plain roentgenogram of the skull.
7. Roentgenogram of the chest (for abscesses and tumors of the lung).
8. Lumbar puncture and examination of the cerebrospinal fluid (cell count, globulin, total protein, Wassermann reaction, colloidal gold reaction, bacterial cultures, smears of the centrifuged sediment).
9. Ventriculography or encephalography.

By accurate interpretation of the data thus obtained, the neurologist plays his part in close cooperation with the neurosurgeon, the internist, the ophthalmologist and otolaryngologist, to the end that an intracranial cause for headache may be established or eliminated.

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## HEADACHES OF NASAL ORIGIN

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THERE is a general misconception among many of the medical profession, as well as most of the laity, that *sinusitis* is a very common cause of headache. This results in many people believing that they have sinusitis because of the existence of a headache. It is especially true of those with a unilateral pain, many of whom have had this diagnosis made by their physician. We see greater numbers of these patients in whom there is no sign of a sinus infection, however, than we do of patients with a definite sinusitis. Too many of them have been on nasal treatments, ranging from simple shrinkage to more or less radical surgery for their supposed sinusitis.

The headaches of *true nasal origin*, although they account for only a small percentage of headaches in general, usually have a *definite symptomatology* and can be diagnosed clinically with a considerable degree of accuracy. For the sake of discussion, I am dividing these headaches of nasal origin into the following groups:

1. Those due to nasal obstruction without actual infection.
2. Those due to sinus infection.
3. Those due to tumors.
4. Those due to neuralgia.

There will be some overlapping of the groups because of the interdependence of the various factors.

**Headaches Due to Nasal Obstruction Without Actual Infection.**—The best known headache of this type is the so-called *vacuum frontal headache*. The term "vacuum" is unfortunate and has resulted in many doubting the existence of

such a headache. It is perfectly true that the body will not tolerate a vacuum, and therefore that there is no vacuum in the frontal sinus. The mechanics of the production of this type of headache is, first, an obstruction of the nasofrontal duct. This is followed by absorption of air from the sinus cavity, but instead of a vacuum, there is a swelling of the mucosa lining the sinus, and there may even be a transudation of fluid into the cavity. Because of this interplay of negative and positive pressures, and the altered state of the sinus, there is a headache over the forehead on the side of the involved sinus. The involved sinus may remain clear to transillumination because there is not necessarily much swelling of the mucosa or much transudation. The *diagnosis* is established by relieving the headache through shrinking the mucosa of the involved side with any of the ephedrine preparations or their substitutes. The majority of the patients who present this picture have unusually large frontal sinuses.

The *cause of the obstruction* may be a high deviation of the nasal septum to that side, an unusually large middle turbinate or one that hugs the lateral wall of the nose, a nasal polyp in the region of the nasofrontal duct, or a nasal allergy. I have seen a number of such patients who frequently have had an attack after swimming and diving. When the obstruction is due to the presence of an acute coryza, it may be the first step toward the development of an acute suppurative frontal sinusitis.

Immediate *treatment* is directed toward the relief of the obstruction by the use of ephedrine solutions or their substitutes. These may be dropped into the nose, sprayed in the nose, or applied directly by the physician. The latter is the most effective, especially if a cotton tampon or cotton-tipped probe soaked in the solution is placed in the region of the anterior end of the middle turbinate. The use of external heat is also very helpful. If there is a tendency to recurrence, the factor or factors which make the obstruction possible should be eliminated. If the condition follows swimming, the patient must either learn how to keep the water out of his nose or he

must give up swimming. If it is due to a high deviation of the septum to that side, the septum should be resected. The mere presence of a deviated septum is not sufficient cause for advising this operation unless it definitely crowds the nose in the region of the nasofrontal duct. The middle turbinate may have to be fractured away from the lateral wall of the nose or its anterior end be removed. Polyps may have to be removed and an allergic investigation and regimen launched.

Although the frontal sinus has received most of the attention in this condition, I see no reason why the *other sinuses* may not enter into a similar situation and produce a headache. The frontal sinus is the most frequently involved because it is the only sinus which has a long duct between it and the nasal cavity. However, I have seen a number of other patients who had severe parietal vertex and retrobulbar headache as the result of nasal obstruction from a marked nasal allergy and polyps obstructing the posterior portion of the nose. Relief was obtained by reestablishing the normal ventilations and drainage of the nose. One patient with a bad nasal allergy and a polyp partially obstructing the posterior nares had severe recurring headaches which were sometimes behind the eye and which frequently produced a pain in the temple that he said could be covered by a dime. Temporary relief was obtained by ephedrine and cocaine to the posterior ethmoid region. After the polyp was removed, the patient had no more such headaches.

Another source of headache or head pain is a badly *deviated septum* which impinges on the lateral wall of the nose. Some may feel that this should be put in the neuritis group, and that may be where it rightfully belongs. If the headache is on the same side as the impingement and is relieved by nasal shrinkage, one is justified in doing a submucous resection. Such a badly deviated septum should be corrected for the sake of the patient's breathing, and it may be the cause of the headache.

**Headaches Due to Sinus Infection.**—These are not nearly as common as is generally supposed. When they do

exist, the diagnosis is easy and certain. They may occur in the early acute stage of sinus infection, or in an acute exacerbation of an old sinus infection. These headaches are *acute* and *throbbing* and are usually *localized* according to the involved sinus: The frontal sinus produces a homolateral frontal headache. The maxillary sinus may produce the same headache as the frontal, or it may produce a pain over the cheek or in the upper teeth. The ethmoids will produce pain in and around and behind the eyes. The posterior ethmoids and sphenoid sinuses may cause a headache in the temporal, vertexial, or occipital regions. The headache is usually *aggravated by leaning over*. It occurs in association with an *acute cold*.

The *diagnosis* is easy and is made by the location of the headache, the presence of a purulent rhinorrhea, careful examination of the nose to determine the source of the rhinorrhea, and the use of transillumination, roentgen rays, and diagnostic irrigation of the suspected sinus. The *treatment* is directed toward clearing up the infection. Chronic sinus infection never produces headache except in the acute flare-ups.

*Treatment of Acute Sinus Infections.*—The treatment of the acute sinus infection, or the acute exacerbation of a chronic infection, is essentially conservative. It is directed toward re-establishing nasal *ventilation* and *drainage*. It is important to put the patient to bed and keep him quiet. Sedatives are used as needed, and he is made as comfortable as possible. Locally, ephedrine solutions or their substitutes are used in the nose. These may be applied as drops, atomizer spray, or on soft cotton tampons placed in the middle meatuses. If drops are used, the patient is instructed to lie on his back across the bed and to let his head hang down over the side so that the medication will find its way into the upper part of the nose. If this is not done, they will run along the floor of the nose to the nasopharynx and accomplish nothing. If the atomizer spray is used, too much pressure must not be produced in the nasal cavity because this may force the infection into other sinuses or into the ears. The soft cotton tampons soaked in the solution and placed in the middle meatus for ten to twenty

minutes produce the best shrinkage. These should be applied gently so as to produce no trauma. Furstenberg<sup>1</sup> advises against even the slight manipulation required to do this. Steam inhalations, either plain or with tincture of benzoin, are very helpful. Heat should always be applied over the involved sinus. Ultra short-wave diathermy may be used, the infra-red lamp being an excellent source for heat. A portable electric bathroom heater is a good substitute, or a large electric bulb with a reflector made out of a tin can may be used.

The sinuses *should not be washed during the acute febrile period*, and adequate time should be allowed after this for them to clear up. If there is still suppuration after about two weeks, the involved sinus should be irrigated and washings repeated every three to four days until clear.<sup>2</sup> The maxillary and frontal sinuses may be treated in this fashion. The ethmoids and sphenoids are treated with suction after nasal shrinkage. The suction should be just strong enough to clear out the secretions, but vigorous suction should be avoided. The *Proetz*<sup>3</sup> treatment is excellent and often obtains results where other methods have failed.

It is a moot question as to whether the *hyperplastic sinus per se* can be the cause of a headache. This is the sinus with a thick swollen mucosa, dark on the roentgenogram and to transillumination, and which returns a clear fluid on diagnostic irrigation. The condition is usually due to an old, healed suppurative process which has resulted in a permanently hyperplastic membrane or to a nasal allergy. When headache is associated with the allergic state and there is no suppuration present, it will respond better to treatment of the allergy than to an operative procedure on the sinus. It is true that some of these patients are relieved of their headaches after a diagnostic irrigation when the water which returns contains no evidence of pus. It seems more logical that this is due to the effect of the warm irrigating fluid on the vasomotor mechanism rather than to the removal of any microscopic evidence of infection.

**Headaches Due to Tumors in the Nose and Sinuses.**—Benign and malignant tumors involving the nose and sinuses

are usually silent until they produce *obstruction, sinus infection*, and definite *pressure on or invasion of a nerve trunk*. Headache, when it does occur, is due to one of the three latter conditions. This is the reason that carcinoma of the sinus is rarely discovered while it is still early. Osteomata are frequently found on routine examination. When small, they rarely cause trouble. It is only when they fill the sinus so as to produce pressure on the walls or when they interfere with its natural drainage that they assume clinical importance.

**Nasal Neuralgias.**—There are two neuralgias of the head which originate in the nose—the *sphenopalatine* or *vidian* neuralgia and the *nasociliary* neuralgia.

*Sphenopalatine or Vidian Neuralgia.*—Sphenopalatine neuralgia was first described and sponsored by Sluder.<sup>4</sup> Later, Vail<sup>5</sup> disagreed with him as to the cause of the condition and the location of the nerve lesion. He described the same syndrome and called it "*vidian*" neuralgia. He maintained that the trouble was in the vidian nerve and not the ganglion, and that the syndrome always means pathology in the sphenoid sinus. The pain in this condition is of a neuralgic character, and usually occurs in severe attacks which have the stabbing character of a tic. It may be a constant pain with acute exacerbations. In distribution, the pain is not confined to the course of any one cranial nerve and may be very widespread. It is usually unilateral. It may occur in the root of the nose and in and about the eye and in the upper jaw and teeth. It usually extends back under the zygoma to the ear and mastoid. It may even spread back to the occiput, neck, shoulder, and, when very severe, to the arm. The arch of the soft palate may be a bit higher on the affected side.

The *diagnosis* is established by relief from the pain on cocaineization of the sphenopalatine ganglion. The nose and sinuses should be carefully examined for exciting causes and any definite cause should be treated. Vail states that these cases are due to a manifest or a latent sphenoid infection. He states that a routine examination is not enough to reveal the trouble and advises careful inspection of the sphenoid recess

with the nasoscope. He also advises diagnostic irrigations and lipiodol injections of the sphenoid sinus.

These cases are not as common as one might be led to suppose by looking up the literature on the subject. That they do exist, there is very little doubt. *Treatment* should be directed to the underlying pathology when it has been definitely demonstrated. We should never indulge in blind operative procedures in the absence of definite clinical findings. Many temporary results may be obtained as the result of shock therapy, but these results are not often permanent. There should be definite evidence of pathology before any operation is undertaken.

When a *facial neuralgia* is present, the sphenopalatine ganglion should always be cocainized as one of the steps in the examination. Relief from cocainization may last for some time and repetition beyond a few times is rarely necessary. It has never been necessary to inject alcohol in cases I have seen.

One sometimes encounters patients with this type of pain who are of a *neurotic* or *hysterical* diathesis and whose pain is relieved by the application of water to the sphenopalatine ganglion. I am not so sure that these are pure hysterias, although they are commonly regarded as such. At any rate, I had one patient who continued to get relief from her pain even after she knew I was using only water. Another patient obtained relief from the application of water if the pain was mild but had to have cocaine applied if the pain was severe. This same patient experienced an increase in the pain when a dry cotton-tipped probe was applied to the sphenopalatine area. One wonders if the relief in these sphenopalatine neuroses and the preceding group of neuralgias is obtained by actual anesthetization of the ganglion, by improved ventilation and drainage of the posterior sinuses, or by an alteration in the vasomotor mechanism.

*Nasociliary Neuralgia.*—This second type of neuralgia has not received much attention. The neuralgia in these cases is confined to the course of the *nasociliary nerve*, which is a branch of the first or ophthalmic division of the fifth cranial

nerve. It may be caused by pathology anywhere along its course; this means in the orbital cavity, the anterior cranial fossa, the ethmoid labyrinth, and the external nose. Mussun<sup>6</sup> reports seeing quite a number of these patients with definite inflammation and dryness of the mucous membrane of the anterior third or half of the middle turbinate. There was no pathologic discharge in the nose. Relief was obtained by the application of cocaine to the middle turbinate. More stubborn and recurrent cases had either a submucous resection or amputation of the anterior end of the middle turbinate done in order to obtain relief.

**Treatment.**—If definite pathology is discovered along the course of the nerve this should be treated. If no obvious cause can be found, one may have to inject the nerve first with *novocaine*, and if this gives relief, to follow the novocaine with *alcohol*. The use of *thiamine chloride* with *nicotinic acid* is giving relief to many neuralgias that formerly required surgery or alcohol injections.

**Summary.**—In treating a patient with a headache or head pain which may be due to some nasal pathology, the nose and sinuses should receive very careful examination. This means not only the routine anterior and posterior rhinoscopy and transillumination, but a careful inspection of the nasal passages with the nasopharyngoscope. The sinuses should be x-rayed and possibly irrigated and filled with lipiodol. First water and then cocaine should be applied to the sphenopalatine ganglion. It is only by such careful and methodical examination that the causes of some headaches are discovered.

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## HEADACHE IN CARDIOVASCULAR DISEASE

JOHN TUCKER

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THERE is some clinical and experimental evidence to show that the headache which may be a major complaint in cardiovascular and renal disease is due to a change in the *dynamics* of intracranial pressure. In this regard it resembles an expanding lesion of the brain, but the increased pressure appears to be due mainly to a high intravascular tension or to edema of the brain. An increase in venous back pressure or a vascular aneurysm may increase the intracerebral pressure, but it is not a common cause of headache. If we agree to the concept that headache is due to a mechanical pressure on or distortion of the dura mater, including its extensions such as the falx cerebri, falx cerebelli and tentorium cerebelli, then it can be conceived that low as well as high subarachnoid pressure could cause the pain. The post-puncture headache due to leakage of spinal fluid through the wound in the dura comes from the low intracranial pressure. Likewise, the enteroptotic, the undernourished, fatigued and hypotensive patient who often is suffering from anemia, may be subject to frequent headaches.

In our experience, however, the patient with cardiovascular or renal disease rarely complains of headache unless the pathologic state produces cerebral edema, cerebral vascular hypertension, or "hypertensive encephalopathy." If a spinal puncture is made at the time of the headache, it will almost always show an increase in intraspinal pressure. Any effective therapeutic measure must take into account the basic factors that produce the headache. Above all, treatment must be directed toward a *reduction in blood pressure* and an *improvement in kidney function*.

In our clinical study and therapeutic measures we must be

certain that the headache is *not due to eye strain*, acute or sub-acute *sinus disease*, *anemia*, or *cysts*, *abscesses* or *neoplasms* of the brain. This calls for a *painstaking history* and *careful clinical examination* in all cases. Often the differential diagnosis is simple, but again it may require special laboratory procedures and roentgenograms.

The headache of cardiovascular and renal disease is *rarely an isolated symptom*. In many instances we find that vertigo, tinnitus aurae, nausea, vomiting, or in more severe states even convulsions and coma, may complicate the picture. On the other hand, since the patient may seek his physician chiefly because the headache interferes with his comfort and well-being, we believe that it is worth while to discuss the clinical states that may produce cephalalgia secondary to disturbances in circulatory and renal function.

**Essential Hypertension.**—In its early stages this disease may produce severe headache in the *occiput*, in the *ocular* and *temporal areas*, or *throughout the skull*. The early morning headache which is relieved by sitting up, by walking about, or by a cup of coffee is a common complaint. The effect of gravity or gastric hyperemia secondary to the digestive process serves to diminish the intracranial blood supply. The relief of headache may persist all day. On the other hand, with any nervous shock, excitement, or sudden physical effort it is apt to return. The majority of these patients are born with unstable vegetative centers. Ordinary daily experiences produce excessive reactions. They worry about nonessentials and the nervous "drive" induces excessive physical fatigue.

**Treatment.**—Therapy of any lasting value must be able to eradicate the cause or to modify the severity of the disease itself. In essential hypertension, the controversy has waged about the influence of the kidneys in producing hyperpiesis. The recent work of Goldblatt with his experiments on dogs raises much hope that at last something fundamental has possibly been discovered. If one diseased or anemic kidney can produce a pressor substance which, in the presence of a second normal kidney, produces generalized arterial hypertension, then

the surgical removal of the damaged kidney can cure the patient. In one case at the Clinic the removal of the damaged kidney caused a striking lowering of blood pressure for several weeks, but the pressure has again reached a high level. Other cases are under observation but the time has been too short for any positive opinion at present. In view of the fact that radical treatment is not available now, we must resort to time-honored methods for the control of essential hypertension and its symptoms.

*Agents given to lower blood pressure* are not particularly successful in relieving the headache. *General measures*, such as rest, modification of the environment and diet, are usually more lasting than those attained by the use of drugs. However, both are important aids.

Nervous *relaxation* is of the greatest value. More rest periods, weekends in bed, frequent vacations at a restful spot, and a simple hobby may help to decelerate the kinetic drive. However, these procedures are not always successful, owing to home conditions, economic pressure, or the anxiety factors incident to the patient's occupation. Under such circumstances we attempt to elevate the reactive threshold by sedation. Moderate *exercise* is very helpful in relieving headache; blood is shunted to the muscles and the vascular tension is lowered. In either case there will be less blood in the cerebral vessels and lower intracranial pressure. A leisurely stroll, a bit of gardening or a mixed foursome of golf, provided that the golf is not competitive, will serve to quiet down the accelerative mechanism.

The use of drugs in the treatment of hypertensive headaches is designed to accomplish one or more of these purposes: (1) *vasodilatation*, (2) *sedation*, (3) as a *specific* remedial measure.

Of the *vasodilators* none has been very successful. The temporary effects of the nitrites, benzyl benzoate, atropine and belladonna, and even sodium thiocyanate, have been of symptomatic value. However, a time always comes when the effect is lost. Of this group, *sodium thiocyanate*, in small doses and

combined with a sedative, gives much relief not only of headache, but also of dizziness and heart consciousness. There is some lowering of blood pressure while the preparation is effective. A good combination consists of equal parts of elixir sodium thiocyanate and elixir phenobarbital, one teaspoonful three times a day. The prescription can be used intermittently with safety.

The most successful of the *sedative drugs* are bromides, hyoscine, and barbital derivatives. These can be used in physiologic dosage, but here again the treatment should not be continued without medical control.

Not infrequently we see patients with manic or depressive states who have acquired hypertensive headaches from the excessive use of sedatives. In sleep, a large dose of sedative is effective in the milder headaches. When insomnia is severe, we may need to use *chloral hydrate*, in 20 to 30 gr. doses by mouth or rectum, or even narcotics. Obviously, *morphine* should be used only in acute severe hypertensive headaches, and *codeine* when the pain is less agonizing. *Gynergen* can be tried by mouth or hypodermically and may be effective as in migraine headaches, but here, too, the administration should not be continuous.

*Diet* in hypertension requires no particular restrictions unless the patient is obese or unless the food is deficient in the vital essentials, such as proteins, minerals and vitamins. It is worthwhile to re-emphasize the fact that, under ordinary circumstances, protein does not harm the kidney or raise the blood pressure. Stimulants, such as coffee, should be used sparingly, moderate indulgence in alcoholics is probably beneficial, and other fluids can be taken as desired.

*Venesection* is of doubtful value in the relief of hypertensive headache.

**Arteriosclerosis.**—The cerebral arteriosclerosis of middle or advanced age rarely causes headache unless it is associated with definite hypertension. In such a patient, a change of posture or sudden exertion may produce a transient headache which is relieved by lying down.

The general features of the more severe headaches are similar to those which one obtains in essential hypertension. On the other hand, when a cerebral accident is impending, there may be a prodromal period of rather severe headache. When a *brain hemorrhage* is anticipated, the patient should be put to bed with heat to the feet and a sedative dose of codeine and bromide or a barbiturate. One may not be able to circumvent the hemorrhage or thrombus, but the amount of bleeding in the former instance may be minimal.

The cephalalgia may be relieved after rupture of a cerebral vascular aneurysm, as illustrated in the following case: The patient, sixty-two years of age, complained of a severe burning behind the inner canthus of the left eye. This persisted for several months in spite of numerous clinical studies and therapeutic measures until he experienced right-sided hemiplegia and partial aphasia. With the rupture of this aneurysm of the left lenticulostriate artery the pain disappeared entirely. While the severe discomfort had not been a generalized headache, yet the patient described it as a headache and came to us for relief. The diagnosis was made after the rupture occurred and not before. An analogous condition may occur in angina pectoris when, after a sudden coronary occlusion, the effort pain may disappear entirely for many months or years.

**Congestive Heart Failure.**—We speak of this condition as an *occasional* cause of headache, not because it is frequent, but because headache may occur during active treatment for myocardial failure. Theoretically, one might anticipate headache as the result of venous back pressure in the cerebral veins. However, the only headache of consequence has come from *overdosage with digitalis*. In addition to nausea, visual disturbance, or abnormal slowing of the heart we note persistent headache. This is relieved by withholding the drug until the excess is eliminated from the body.

As in congestive heart failure, many miscellaneous conditions which give rise to increased venous pressure in the head and neck rarely cause headache. These include *mediastinal tumor*, *intrathoracic goiter* with compression of the superior

vena cava, or any abnormal condition which *impedes the venous flow from the cerebrum to the heart.*

**Spontaneous Subarachnoid Hemorrhage.**—We speak of this particular cerebral accident since it gives rise to the most severe headache and may simulate meningitis. It is not usually the product of longstanding hypertension, but rather of rupture of a congenitally weak spot in an artery of the circle of Willis. There is massive hemorrhage in the basilar cistern and in the subarachnoid space. This produces both increased intracranial pressure and meningeal irritation.

The *treatment* is rest and sedation by codeine or morphine. Cold to the nape of the neck may add to the patient's comfort. One hesitates to advise a repetition of the diagnostic lumbar puncture since it may encourage further bleeding. However, in many cases it is safe to repeat spinal drainage every few days to reduce the pressure as low as 100 mm. of H<sub>2</sub>O if the amount of blood in the fluid becomes less and if it relieves headache and restlessness. Time appears to solve this problem—the patient usually dies from a second hemorrhage in a few months or years. An attempt by Dr. W. J. Gardner, of our neurosurgical staff, to strengthen the thrombosed area in the bleeding artery by a strip of muscle did not prevent a recurrent hemorrhage in the one case in which it was tried. The second and fatal hemorrhage occurred about five months after the operation.

**Conclusions.**—This brief review of certain types of headache which occur as a major symptom in hypertensive cardiovascular disease is of necessity incomplete. We have drawn attention to the symptomatic importance of an abnormally high or a low intraspinal pressure. It would appear from clinical and laboratory studies that this disturbance of pressure dynamics can be produced by intravascular hypertension, cerebral edema, or cerebral anemia secondary to intracranial vascular spasm. Simple therapeutic measures can be employed to relieve the headache even though the pathologic changes in the vascular and renal functions are not amenable to treatment. On many occasions the relief of pain will produce better rest and relaxation and, in this way, prolong the life of the patient.

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## HEADACHE FROM ARTERITIS OF THE CERVICAL SPINE

C. L. HARTSOCK

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A CHARACTERISTIC type of headache is frequently caused by arthritis of the cervical spine. In the osteo-arthritic age group, this form of headache ranks in frequency with ocular and migraine headaches. Frequently it is the first sign of a more generalized arthritis, but because the pain masquerades more as a cephalalgic one than as an arthralgic one, the true etiologic character of the headache is overlooked and often attributed to other factors. Fortunately, the history is quite characteristic in most cases, and is typically diagnostic as the true migraine syndrome.

The headache invariably begins in the occiput, but it has a tendency to spread upward and forward into the temporal regions as it becomes more severe. If the patient is able to analyze critically the onset, the pain will really be placed in the cervical muscles with a feeling of stiffness and soreness, especially of the attachment of the trapezius muscle to the skull. Of extreme diagnostic importance is the *tenderness* of this tendon attachment. The headaches occur periodically at first, lasting three to four days, a trifle longer than the usual migraine headache. There is a tendency to have *long seiges* of constant headache which may become a *permancnt* daily headache. In a great majority of cases the headache comes on early in the morning and usually wakens the patient from sleep.

Most patients notice the relation of the headache to *exposure to drafts*, such as riding in the back seat of a car, sitting in an air-cooled movie, and following wetting of the hair, especially if there is also a draft on the head while it is wet. Drying the hair with dryers often brings on the headache. Another

common cause is anything that will induce *tenseness of the muscles of the neck* for a long period of time, such as driving a car for long distances, sewing, stenographic work, etc. If there is an associated eye muscle error, focusing the eyes for long periods of time is doubly liable to cause the muscles of the neck to be more tense.

The *indirect* cause, such as drafts, wet hair and eye strain, sometimes occurs the previous day and is frequently overlooked unless attention is directed to this, and then the relationship can usually be recalled. Sometimes, even the removal of a small amount of protection from cold, such as when a man has his hair cut, is enough to cause this myalgic type of headache.

*Crepitus* frequently accompanies the headache and is audible when the head is turned from side to side. Flexing the head forward and stretching the neck muscles increase the pain. Frequently there is a characteristic motion of bending the head backwards and, with the palm of the hand, stroking the back of the head with a downward movement towards the neck. This usually gives some relief. Many patients have learned that *heat* and *massage* will give great relief. As a rule there is no associated nausea and vomiting.

The headache occurs mostly in *elderly* people who are approaching the osteo-arthritic age group, but occasionally some patients in the early twenties are seen. In such patients there is more possibility of an infectious process being present whereas, in most patients, the arthritic process seems to be of the metabolic type related to osteo-arthritis. If the patient is over fifty years of age, there usually is fairly marked *roentgen evidence* of this type of arthritis in the cervical spine. A history of arthritic pains in either location, especially the lower back, knees and shoulders, is further confirmation of the nature of the occipital headache.

There will be minor variations in different cases, but there always will be enough salient features on the basis of the *history* alone to separate this type of headache from the great group of cephalalgias.

When the headache persists for long periods of time, or if it eventually becomes constant, it can be a major cause of disability. In persistent cases, intracranial lesions are frequently suspected and this incurs great expense and suffering in efforts to seek the etiology.

Owing to the frequent association of hypertension and osteo-arthritis in the same patient, the headache is frequently attributed to hypertension. I do not mean to imply that there is a causal relationship between hypertension and osteo-arthritis. They are both degenerative diseases of age and both occur more commonly in the older age group, especially in more obese individuals.

If this type of headache can be so easily recognized from the history alone, and possibly from simple examination of the cervical region, what other examinations are indicated to help in the solution? The investigation should first be directed along the usual lines for arthritis. Obvious *foci of infection* should be removed, but the fallacy of considering osteo-arthritis as an infectious disease and attempting to treat it as such cannot be emphasized too strongly. *Chemical and metabolic studies are important.* An increased glucose tolerance, suggestive of a mild diabetes, sometimes is present and is most helpful in the dietary management.

A *low basal metabolic rate* is the rule, and again a clear indication for therapy that is most beneficial. In selected cases, the *blood uric acid* should be studied. Studies of the *gastro-intestinal tract*, especially for colonic and biliary stasis, are often helpful in outlining a successful therapeutic regimen. Achlorhydria may afford an excellent clue.

*Examination of the eyes* should never be omitted in any case of headache and should be done in this type although, in reality, this is not a true headache. Refractive errors may be a factor, but of great importance is careful measurement of the muscle balance. The muscles are definitely unbalanced in a high percentage of cases. It might be said, then, that this headache is strictly an *ocular* headache, but there is too much evidence that the eyes act only as an aggravating factor in

focusing strain on the cervical muscles and determining the site of election for the arthritic process.

Since the treatment of periodic headaches has been so notably aided by allergic management, the question often comes up concerning the advisability of studying these patients from an *allergic* viewpoint. We have been disappointed in the results of allergy studies in this type of headache and no longer advise them unless the patient is a proved allergic individual in other respects. Dr. Thomas discusses this angle more completely at the beginning of this symposium.

One of our patients formerly had definite migraine, with nausea, vomiting, and unilateral frontal headaches. This type of headache then ceased and the typical arthritic headache developed. Foods that formerly brought on the sick bilious headache would also precipitate the occipital headache, but avoiding these foods would not prevent other causes from bringing on the occipital headaches. Caution, of course, usually dictates that these patients should have a *spinal puncture* to rule out the many causes for headache over the diseases of the central nervous system. Eventually, however, one gains almost enough confidence in clinical judgment to forego this expensive and at times incapacitating study.

*Roentgen examination of the cervical spine* may, as mentioned before, reveal an osteo-arthritic process, but its absence does not affect the diagnosis when all the other evidence is positive.

**Treatment.**—Treatment should be both *preventive* and *palliative*. All causes of *excessive fatigue* should be eliminated as far as possible. Care should be taken to avoid drafts. This may be done by having the patient wear a wool covering over the back of the neck when exposed to drafts, especially during sleep. *Eye strain* should be avoided, and muscle errors corrected as far as possible by exercises, glasses and muscle operations. When the patient knows of definite causative factors, a small amount of acetylsalicylic acid at bedtime will often prevent the headache. If the headache develops, *heat* and *salicylates* administered early will often give quick relief; if delayed, they are frequently futile.

*Heat and massage*, especially the more constant type, are of utmost value. *General arthritic measures*, such as a low carbohydrate diet with increased vitamins, especially vitamin B, a reduction in weight if obese, anti-constipation measures, and mild salines in certain cases, are all helpful and useful measures. We have observed some help from *cholagogues*. *Desiccated thyroid* should be given in tolerance doses. *Cinchophen* even should be used in some of the more difficult cases; however, care should be taken in the administration of this drug.

The improved forms of *physiotherapy* offer the most help to these patients. *Orthopedic measures*, such as continued head traction, are necessary in obstinate cases. The prognosis is entirely in relation to the frequency and severity of the headaches and the ability of the patient to undergo treatment—just as in any case of arthritis.

**Summary.**—I have directed attention to one of the very frequent causes of headache which, because of its very nature, is frequently overlooked as the true etiologic factor, the headache resulting therefrom often being attributed to other causes. Besides the relief that can be obtained by approaching this type of headache on the basis of its true cause, it is amazing the amount of relief the patient experiences from a psychologic viewpoint when he feels he knows the exact cause of his headaches. Many worry about brain tumors, strokes, and all other such possibilities as enter the mind. The chronic headache problem becomes a much easier one when this large group can be separated off without too much diagnostic difficulty.



## HEADACHE AND HEAD PAIN OF OCULAR ORIGIN

A. D. RUEDEMANN

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Two important facts in conjunction with headaches and head pain should be remembered: (1) The eye physician should not divorce the eyes from the rest of the body; and (2) the general physician should not divorce the eye physician from medicine.

Headache is the most common complaint appearing in one hundred histories, either picked at random or consecutively. It is the one complaint that is used by many drug concerns to build up fortunes. There is more treatment for headache than for anything else; more people consult doctors because of this symptom, and many physicians live well because of their ability to ease the "run-of-the-mine" type of headache. It is the great social excuse to evade undesirable engagements and, without it, many people could not exist.

Because of the variety of pains and aches and the wide range of severity, it is extremely important to allow the patient to tell his or her story. One can frequently judge whether the headache is functional or organic by the manner of telling the story and the amount of time required, as well as the measures necessary, to relieve a headache.

It is unnecessary to draw any medical man's attention to the constant overuse of the eyes—the almost continuous visual effort from early morning until bed time, and then that final chapter of a story under poor light when the day is over. When you consider this fact, you can realize that the eyes must be well prepared, both physically and mechanically, to do the job that is expected of them, and this job becomes more exacting daily.

*Unilateral headache or head pain* is caused by the eyes only when a single eye is involved. In the absence of inflammation, the cause may be ciliary spasm, a localized neuralgia, or spasm of a single muscle. With inflammation, we have cases of iritis, iridocyclitis, uveitis, glaucoma, and other localized inflammatory processes. It is well to keep these in mind, for only recently I saw a woman who had severe unilateral pain with a slightly inflamed eye and only slight iritis but a definite low-grade glaucoma. She had been under treatment for nine months and she was completely relieved by eserine salicylate.

Pain from ocular or orbital *inflammation* is not always localized in the orbit. It is often referred over the side of the head, behind the ear, and down the neck. It need not be associated with the use of the eyes although use tends to aggravate it. However, unilateral head pain is not commonly ocular in origin. I mention it here to draw attention to it as a possibility.

*Bilateral pain*, whether frontal, vertex, bitemporal, occipital, suboccipital, or over the tip of the mastoids, may be ocular in origin. It may be as mild as a zephyr or as severe as that of a cerebellar tumor, and until the patient has been examined by someone who will take the time to do other than hand him a pair of glasses, he is being misled. A pair of glasses is not a diagnosis, nor is it always the answer to the problem of headache. Until one can safely say that the refractive error is the cause of the patient's difficulty, the patient is entitled to a *thorough study of the muscle balance*, a *visual field examination*, and one or more *tension readings*, as may be required. The patient will be examined as carefully as you wish him to be—the better the examination, the more frequent the right diagnosis.

*Nearsighted* people do not have headache or head pain unless the nearsightedness is unequal or severe, or unless they are abusing their eyes. It is true that people with myopia have difficulty when they are outside looking long distances or when in very bright light, and this exposure may produce headache. We see numbers of people who watch air races and either for-

get to wear dark glasses while peering skyward or deem it unnecessary. This may produce severe headache, nausea and vomiting, and almost complete collapse.

If one takes a nearsighted individual and mixes the nearsighted error with a muscle error, you may have trouble, and this is true of farsightedness as well.

*Farsighted people* are apt to have frontal headache which is moderate to severe in character and presents itself almost daily in the afternoon or evening. It sometimes is definitely associated with certain types of work. The diagnosis is easy to make and the treatment is a pair of glasses used therapeutically, not as an aid to vision.

If there is an inequality in the amount of error per eye, the pain may be more severe over one eye.

*Errors in refraction* usually produce frontal, vertex, or bi-temporal pain which may be associated with slight dizziness. Nausea is usually relieved by going to bed or resting or taking a single aspirin tablet. It is made worse by sewing, playing cards, and other close application. An error of refraction *associated with a muscle error* is almost certain to produce symptoms of headache, such as pain or nervousness, irritability, exhaustion, nausea (rarely vomiting except in extreme cases or abuse), loss of weight, etc. You cannot be certain about a patient's muscle balance unless the eyes have been thoroughly checked and, further, you cannot be sure of it then if he happens to have some constitutional disease such as hyper- or hypothyroidism, Parkinson's disease, encephalitis, or diabetes.

*Muscle operations and exercises* are not the whole answer. Many patients are improved by proper correction of the eye muscles, either surgically or by treatment, but it must be carried to completion. Halfway measures only tend to increase the difficulty. Patients who give a history of having undergone previous eye muscle surgery or treatment should be carefully checked. The nausea and mild gastric upsets so frequently associated with muscle imbalance, as evidenced by *car-sickness, shopping headaches, and bridge-party nervousness*, can be benefited, and in those people who have repeated gas-

tric surgery for questionable adhesions, the eye muscles must be considered as a possible cause of symptoms. The oculo-gastric reflex is an active irritating one and may mislead or cloud the diagnosis. Pain due to eye muscle imbalance is frequently along the superior or inferior nuchal lines or at the tip of the mastoid where the sternocleidomastoids are attached. *Neck pain* is more frequently due to ocular muscle imbalance than anything else. The neck muscles function primarily to move the head so that the eyes will be in a position to see.

There is a definite *periodic increase* in head pain of muscle origin. It usually becomes more frequent in October and is well on its way in December, reaches a peak in January and falls off in the spring when the days become longer and outdoor exercises become the custom.

Every child, before entering the first grade, should have his eyes refracted under atropine, so that he can be protected against abusing a pair of inadequate or deficient eyes. The girl with the nervous breakdown, the child who is inattentive, the person in business who has a headache at noon which is relieved by lunch, and then has a recurrence about three or four in the afternoon, the clock-watcher, the student who cannot concentrate, the convalescent patient who has headache and is reading in bed—these and many others belong to the group of people who have faulty, poor, or inadequate eye musculature. They may require *exercises, surgery, or glasses*, or all three.

I can also tell you that many of these patients require *medical treatment* for a deficiency in thyroid or vitamin A. Some have general muscle exhaustion due to menopausal disturbance or some cerebral disturbance. It is well to remember that a patient with ocular muscle imbalance may have his primary disturbance elsewhere, the muscle trouble being secondary and the pain a tertiary portion of the entire picture. It is well to think of these patients as sick people who need more than a pill—they need careful study and definite management. Anything short of this fails to relieve the pain.

In closing, let me remind you again that *neck pain, gastric*

*upsets*, and *severe symptoms* are frequently due to *ocular disturbances*. The eyes start out in life with the individual—they may be faulty to start with or they may become faulty through abuse or disease, but they are ever present and constantly abused. They are necessary for the enjoyment of life, and when life reaches the ebb, their use should be a comfort and a pleasure. In order to keep the eyes in perfect condition, every branch of medicine is necessary. A faulty diagnosis may lead to blindness or death, frequently to an unhappy and cantankerous patient, whereas with a little care and proper direction, the eyes will carry on without a great deal of trouble.



## HEADACHE OF GASTRO-INTESTINAL ORIGIN

C. L. HARTSOCK

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HEADACHE is recognized as a symptom frequently resulting from disorders in various parts of the body, the mechanism of the painful sensations and its relation to the primary disorders being quite obscure. That disorders of the gastro-intestinal tract should be a common cause of headache would seem to be a plausible conclusion. Such conclusions seem even more plausible when it is observed how frequently headaches and gastro-intestinal disturbances are so closely associated. A cause and effect relationship would certainly appear to exist.

The patient's reasoning and analysis of his symptoms invariably leads him to the belief that the headache is in some way caused by the digestive disturbance, whereas the physician's training and experience tell him that the reverse is more often true: That is, the *gastro-intestinal upsets and dysfunctions* that *precede, accompany, or follow* the headache are more likely to be an *associated disorder than a causative factor*. The following facts and observations are the ones that usually lead patients, and sometimes physicians, to believe that there is a causal relationship between headaches and digestive disorders:

*Nausea and vomiting* are frequently observed in relation to headache, especially the so-called migraine or bilious type of headache. The term "bilious headache" undoubtedly originates from the fact that so many patients who have nausea and vomiting associated with headache continue to vomit until they bring up a dark green bitter bile, after which they begin to have immediate relief. What is more natural than to assume that the headache is the result of some gastro-intestinal disorder, and probably that the disorder is in the biliary tract?

Cause and effect appear so obvious in such cases that a careful scrutiny of facts is necessary to make any other interpretation. The close observer, however, notices that the headache invariably *precedes* the nausea and vomiting, and the logical deduction should be that the nausea and vomiting are caused by the *same etiologic factor that caused the headache*.

The self-evident fact that intestinal excreta are filled with germs, malodorous aromas, and putrefactive poisons has also led to the very plausible theories that *retention of such products of digestion in the body more than a certain number of hours would lead to sundry and horrible afflictions*. Headache is especially included in this category of ailments caused by auto-intoxication resulting from *colonic stasis*. The great number of patients who resort to innumerable washings and flushings of their intestinal systems to prevent or relieve their headaches offers strong evidence that in some way there is a causal relation between the two. We also have the experience of those patients who always get a headache if they overeat, or if they go too long without eating, or who react to the ingestion of certain foods or foods prepared in a certain way. Some patients are relieved of headache by *hot food and fluids*.

Such experiences certainly, if true, suggest that many headaches are in some way related to disorders of the gastro-intestinal tract. It is my belief, however, that a proper interpretation of the above statements would lead to different conclusions. I believe that in most cases the gastro-intestinal relationship of symptoms is *secondary* to other factors causing the headache or to the disturbance in the central nervous system itself. While I do not want to leave the impression that some headaches cannot be caused by toxic states resulting from faulty elimination habits, I do want to emphasize the fact that each case requires a careful analysis of cause and effect. With this in mind, I have been accustomed to view such problems as having three possible solutions or conclusions: First and foremost, the headache should be considered as being *primarily in the central nervous system*, with the gastro-intestinal symptoms secondary. Second, the disease or toxic agent may be

entirely outside either domain, with resulting *reflex symptoms* produced in both. Third, and I believe least likely, the headache may be a true manifestation of some *organic* or *functional* gastro-intestinal disturbance.

The solution of many headache problems requires the services of specialists cooperating closely with an internist who has a broad viewpoint of the whole bodily domain. The specialist in any field, and this applies also to the gastro-enterologist, is prone to view all human ills from his narrow viewpoint, and unless he trains himself to think of and eliminate other possibilities before he concentrates on his own field, he will often miss the true solution of a problem. Many patients consult the gastro-enterologist because of a belief that the origin of the headache is in his field. I believe the problem of headache should never be approached with the idea that it is secondary to some gastro-intestinal condition until other examinations have been completed and more specific causes ruled out. The *oculist*, *neurologist*, *allergist* and *syphilologist* have a *prior claim* on the headache patient with associated gastro-intestinal disturbances before his problem becomes primarily a gastro-intestinal one.

A minimum routine *neurologic study* should include a study of the fundus for evidence of increased intracranial pressure and vascular changes. A study of the pupillary reactions gives the most helpful clues to the diagnosis of syphilis of the central nervous system. Similarly, the reflex actions, station and gait are important. The level of the blood pressure, the cardiovascular findings, the number of blood cells and hemoglobin content, and urine and complement fixation tests, may give clues as to the origin of the headache and digestive upsets.

As the internist conducts these examinations he will often find that the leading clue will suggest the proper specialist to whom the patient should be referred for further examinations. If the exact cause of the headache is not suggested by the results of the internist's examination, the next step to offer the most help is a consultation with the *oculist*. His study should include not only a refraction, but a careful measurement of the

ocular muscle coordination and readings of the intra-ocular pressure. *Ophthalmologic study* is of the utmost value to the internist in ruling out those organic diseases of the eye and central nervous system in which it is so important that no delay be made in the diagnosis. This study is often the deciding factor as to whether the neurologist should be consulted.

*Allergy* is probably the chief cause of coexisting headaches and gastro-intestinal symptoms, and a careful inquiry should be made in regard to manifestations of allergy in the patient and his relatives. However, examinations of the allergic state are so indefinite as to the exact role allergy plays in causing any manifestation, and so much time elapses before the trial and error method of treatment proves the allergic character of the headache, that I believe all possible causes of headache that might be seriously affected by delay should be eliminated before the patient is transferred to the allergist.

Only when the presence of *brain tumors, infections of the central nervous system, cerebral arteriosclerosis, refractive and muscle errors of the eye, hypertension, uremia, cardiac decompensation, lead poisoning, syphilis, hypothyroidism* and obvious allergy as cause of headache with gastro-intestinal symptoms are ruled out, should attention then be directed to the gastro-intestinal tract.

The *functional* disturbances, rather than organic diseases of the gastro-intestinal tract, are by far the more common causes of headache.

The most definite *organic condition* of the gastro-intestinal tract that produces headache is high intestinal obstruction of a mild and periodic character which leads to a state of *alkalosis*. Such obstruction is more apt to be below the pylorus, leading to duodenal stasis, but obstruction at the pylorus even without vomiting can produce an alkalotic state. Duodenal ulcer, being the most frequent cause of pyloric obstruction, lends itself nicely to producing an alkalotic state through the use of alkalis so commonly used in the treatment of the ulcer symptoms. It is impossible to distinguish the type of headache produced by the *periodic alkalotic state* from a true migraine on the

basis of history alone. Migraine being so common and high intestinal obstruction so rare, it seems impractical to suggest a gastro-intestinal roentgen study in all cases of migraine-like headaches, simply to find the occasional obstructive case. Patients with periodic headaches and vomiting associated with anemia and elevated blood pressure should, however, always have blood chemistry and gastro-intestinal roentgenogram studies. The treatment of such headaches is naturally the relief of the intestinal obstruction or the withdrawal of alkaline medication.

*Biliary tract disease*, as mentioned previously, is thought to be a frequent cause of headache. I believe, if the truth could be known, that alteration in function of the liver does play a large role in headaches, especially of the allergic variety. I believe the liver is an important factor in conditioning the absorption of unchanged protein molecules from the intestine into the blood stream, and one must assume that this is the probable mechanism of allergic headaches.

Biliary tract disease as we can prove it, cholecystitis and calculous disease, is seldom the cause of headache and rarely are headaches cured by the removal of a diseased gallbladder. It has been my observation that many patients have been subjected to *gallbladder surgery* on the clinical evidence of vomiting bile and abdominal soreness that is often associated with *migraine*. It is true that this occurred more frequently before the days of accurate gallbladder visualization, but the idea is still prevalent and the patient still receives such suggestions for treatment. This, probably more than the search for high intestinal obstruction, would constitute a good reason for doing a *routine roentgen study on the gastro-intestinal tract*, if only to convince the patient of the fallacy of such methods of treatment. Of course no criticism is made of operating for the relief of definite pathologic conditions of the biliary tract, especially when local symptoms are present, but when the major symptom is headache, one should be very careful about the prognosis of relieving the headache by gallbladder surgery.

*Achlorhydria* may be a conditioning factor in headaches

through the anemic and fatigue states that is so likely to cause.

*Cecal stasis* is often caused by organic diseases such as adhesions and congenital bands. It has been my clinical impression that neuralgic states of the head, more than typical headaches, are prone to occur with obstinate cases of cecal stasis.

*Acute febrile states* involving the gastro-intestinal tract, notably typhoid fever, are frequently ushered in with severe headache, but that seems beyond the purpose of this paper which deals only with the chronic headache problem.

On the borderline between organic and functional gastro-intestinal tract disease as a cause of headaches falls that large group of patients who insist that they have headache associated with *constipation*. They usually are convinced that if a bowel movement does not occur every twenty-four hours, a headache results. Such patients are slaves to the cathartic or enema habit, and are difficult patients to handle from a therapeutic standpoint. The cause of such headaches is not very well understood, but is ascribed to "auto-intoxication," which in itself means little or nothing. A more satisfactory explanation is that the patient is allergic to the end products of digestion or more likely to the bacterial flora of his own intestinal tract. The absorption of toxic products of putrefaction and fermentation must also be considered. Even more probable than these theories is that the headache is only a part of the same functional neurogenic disturbance that causes the constipation.

Gastro-intestinal studies in such cases usually reveal an irritable bowel of the spastic type, but there is of course nothing specific about this in relation to headaches, as most nervous patients show the same condition. Stool cultures are not remarkable for any particular type of organism, but in obstinate cases the patients' sensitivities to various bacteria should be tested by intradermal tests. Suitable vaccines should be administered if the patient is found sensitive. As a rule, the establishment of natural elimination without catharsis or enemas, by the principles of treating irritable colon, will give relief in many cases.

A certain group of patients who apparently have this syndrome have failed to respond to any form of therapy of any physician they have consulted. Many such patients have become addicts to acetanilid-containing drugs as the only means of securing relief and frequently as a result of the acetanilid and constipation develop *sulfhemoglobinemia*.

Another type of headache in which the gastro-enterologist can be of great assistance occurs in those individuals who have a *poor constitution*, who are *chronically tired* and who usually complain of a great deal of *indigestion*. The headache in these cases probably is not caused directly by the indigestion, but rather by *fatigue*. Very little relief, however, is obtained by treatment unless the patient's general condition is improved, and this rarely occurs unless the digestive symptoms are adequately treated. A high vitamin, high caloric diet with frequent small feedings, regulation of the bowels, adequate rest, mild and limited exercise, physiotherapy, sedatives and psychotherapy usually will correct the digestive disturbances, add weight and strength, and with the improved general condition, the headaches will disappear.

In general it might be said, therefore, that while the gastrointestinal tract is infrequently the direct cause of headache, the gastro-enterologist can contribute a great deal in the treatment of some vague and obscure headaches. This is particularly true of migraine which does not respond to simple allergic management. The institution of a low carbohydrate diet, bowel management, periodic duodenal drainage and administration of bile salts are of great value in certain selected cases—the selection being purely on a trial and error basis.

#### CONCLUSION

In concluding the discussion of headaches of gastro-intestinal origin, it can be stated that, with the exception of the headache due to alkalosis and high intestinal obstruction, the whole subject is very vague, and full of theory and ideas that appear as unscientific as the claims of the diet faddist and the colon irrigationist. It must be remembered, however, that we

are therapists as well as scientific diagnosticians, and if in any way we can contribute to the therapeusis of the headache problem by correction of organic or functional disorders of the gastro-intestinal tract, we should not hesitate to do so because of apparent scientific discrepancies between cause and result.

I do want to emphasize, however, that it is the duty of every specialist—and this applies especially to the gastro-enterologist—to look for other, more definite causes of headache far afield from his immediate interest before concentrating on indefinite causes in his own narrow domain.

## HEADACHE OF SYPHILITIC ORIGIN

E. W. NETHERTON

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BECAUSE of the tendency of *Spirochaeta pallida* to invade the central nervous system, it is not surprising that syphilis is one of the important causes of headache. Headache is frequently the *chief symptom*, and at times the *only complaint*, which brings a syphilitic patient to the physician. Headache of syphilitic origin occurs during the early and late stages of the disease. It may be accompanied by other symptoms and clinical manifestations of the disease, but it is not uncommon, particularly in late syphilis, for headache to precede for a long time the appearance of neurologic signs produced by syphilis of the central nervous system.

Headache of syphilitic origin is due to an inflammatory reaction of a specific nature involving the meninges, the arteries of the brain, or both structures. There is nothing pathognomonic about the headache which is due to syphilis. However, the physician who is syphilis conscious and whose clinical acumen is of high degree will consider syphilis as a *possible etiologic factor* in all cases of severe headache for which *no cause has been discovered*.

**Symptoms.**—Headache caused by syphilis of the central nervous system may be slight, or it may be a major symptom. When it is severe, it is dull, stupefying, and usually diffuse in character. The *site of greatest intensity* may be in the frontal or posterior orbital region or in the occiput, but it is seldom localized to one small portion of the head. Syphilitic headache is most often *intermittent*. It may occur every day or two or three times a week, only to disappear for weeks or months and reappear again without any apparent cause. There is a popular belief that headache caused by syphilis most often oc-

curs. at night. It is true that occasionally the patient complains of being awakened at night by a severe headache. However, *nocturnal occurrence is not a constant characteristic*. Stokes and Garner<sup>1</sup> state that the tendency of a syphilitic headache to occur at night has been exaggerated. In a discussion of the symptomatology of cerebral syphilitic endarteritis, Nonne<sup>2</sup> states that headache may be very severe and it may, but not always, be worse at night.

A patient suffering from headache of syphilitic origin may complain of *other symptoms* which should arouse the suspicion of the alert physician as to the true cause of the patient's illness. Among the more common accompanying symptoms are *dizziness of an intermittent type, nausea, vomiting, insomnia and psychic disturbances*. The patient may be irritable, or at times dull and stupid and unable to work efficiently. The personality changes may, in some respects, be similar to those observed in paresis. However, it should be pointed out that headache is seldom an important symptom in a case of well established paresis. Patients with cortical meningitis may complain of a pressure sensation on the vertex of the head and palpation of the scalp will show the presence of small, localized areas of hyperalgesia.

**Headache of Early Syphilis.**—Headache which occurs in early syphilis either accompanies the secondary eruption and the mucocutaneous relapses, or appears during the period of the first four years of the disease which is thought to be required before latency of the infection becomes established. In early syphilis, the type of involvement of the central nervous system is most often predominantly meningeal, although serious involvement of the vascular elements of the central nervous system may occur during the early months of a syphilitic infection.

In the evaluation of the importance of headache in acute syphilis, it is necessary to consider the *severity of the pain, the associated neurologic signs, the type and amount of treatment* which the patient has received before the onset of the headache, and the *abnormal findings in the spinal fluid*.

It is not uncommon for patients with *untreated secondary syphilis* to complain of headache when questioned specifically regarding the presence or absence of this symptom, although headache is not often the major complaint. Stokes and Garner<sup>1</sup> state that headache is an important symptom of secondary syphilis, and in a tabulation of the symptomatology of early constitutional syphilis, they record headache in 24 per cent of the cases. Occasionally a patient with secondary syphilis seeks relief from a diffuse, more or less constant headache, stiffness of the neck and pain in the long bones, while at the same time failing to consider an associated mucocutaneous eruption of significance.

It would seem most likely with the wide dissemination of the *Spirochaeta pallida* during the spirochetanemia of early and late secondary syphilis that, in the majority of patients, the *neural axis* would be invaded by the spirochetes. However, examination of the *cerebrospinal fluid* of patients with early syphilis shows that the central nervous system is invaded in approximately 20 to 30 per cent of the cases. Wile and Marshall<sup>3</sup> found that in 236 cases of primary syphilis the cerebrospinal fluid showed a pleocytosis in 16.1 per cent, an increase in globulin in 19 per cent, and a positive Wassermann reaction in 5 per cent of the cases. In 508 cases of secondary syphilis, there was a pleocytosis in 34 per cent, an increase in globulin in 35.1 per cent and a positive Wassermann reaction in 26.5 per cent. It is significant that in the same study these observers found that in 568 patients which were classified as latent syphilitics, the spinal fluid was abnormal in 28.6 per cent of the cases.

Moore<sup>4</sup> states that 20 to 35 per cent of all patients with early syphilis have involvement of the central nervous system and that the patient who escapes early involvement of the neural axis usually will not develop late parenchymatous neurosyphilis. In a later study Moore<sup>5</sup> found that "in late syphilis of all types, excluding clinical neurosyphilis, the incidence of asymptomatic neurosyphilis was 13.5 per cent."

The Cooperative Clinic Group<sup>6</sup> found that, without consid-

eration of the time when the lumbar puncture was made or of previous treatment, *abnormal cerebrospinal fluids* occurred in 23.8 per cent of the cases with seronegative primary, 29.8 per cent of seropositive primary, and 34.1 per cent of early secondary syphilis. In late secondary syphilis the fluid was abnormal in 56.1 per cent of the cases. They also observed that in untreated early secondary syphilis clinical neurosyphilis was recognizable in only 1.7 per cent of the cases.

These observations point out that as the clinical manifestations of early syphilis disappear, either spontaneously or as the result of antisyphilitic therapy, the foci or syphilitic inflammation in the various tissues decrease in intensity, and when latency has become fully established, approximately 70 to 80 per cent of the patients *will have normal spinal fluids* and will *probably escape late parenchymatous neurosyphilis* (paresis and tabes dorsalis). However, some of the patients may later develop late syphilis of the central nervous system of the vascular type.

In the remaining 20 to 30 per cent of untreated or inadequately treated cases of early syphilis, the spinal fluid does not become and remain permanently normal with the disappearance of the early manifestation of the disease. The disease is clinically latent but, in reality, these patients have *asymptomatic neurosyphilis* and may remain free of signs and symptoms of syphilis of the central nervous system over a period of time varying from a few weeks or months to several years. It is from this group of patients that the late *meningovascular* and *parenchymatous neurosyphilis* is derived. Also, it is now well established that the syphilitic patient who is apt to develop paresis or tabes dorsalis in the future can be detected with some degree of accuracy by the *type* of spinal fluid which he has during the first two or three years of his infection. Therefore, in the proper management of acute syphilis, *routine examinations of the spinal fluid* are as important as the changes in the blood serologic reactions for determining the efficacy of antisyphilitic therapy. Likewise, the initial investigation of every case of latent syphilis should include an ex-

amination of the spinal fluid. The investigation of all types of late syphilis should include an examination of the spinal fluid, provided the age of the patient or other factors do not contraindicate this procedure.

This brief reference to asymptomatic neurosyphilis may seem not to be apropos to the subject. That is partially true; however, a patient with asymptomatic neurosyphilis may either develop headache without any apparent reason, or following *severe trauma* to the head. Trauma may activate a syphilitic meningitis; therefore, the possibility of syphilis as a cause of posttraumatic headache should always be kept in mind. It is obvious that the physical findings, the severity of the trauma, and the spinal fluid findings must be correlated as the activated neurosyphilis might be complicated by a subarachnoid hematoma or other serious injury to the brain.

In early syphilis, *acute meningitis* and *neurorecurrence* are the most serious types of neurosyphilis in which headache is usually a prominent and distressing symptom. The pathologic changes observed in these two conditions are identical; however, the explanation of the mechanism of their production differs. Acute syphilitic meningitis is rare and usually occurs during the early stages of the disease in an individual whose body defense reaction is unable to protect the nervous system from an overwhelming invasion and involvement by the *Spirochaeta pallida*. Neurorecurrence is much more common. It has become common since the advent of modern chemotherapeutic remedies. It is a product of the arsphenamine era.<sup>7, 8</sup> Neurorecurrence is a relapse involving the central nervous system. Inadequate and injudicious arsphenamine therapy not only fails to eradicate completely the spirochetes located in the nervous system, but also interferes with the patient's own bodily defense reaction which, when unaltered by treatment, is in most cases of early syphilis sufficient to protect the patient from serious and permanent involvement of the central nervous system. Neurorecurrence may occur when the patient is receiving antisymphilitic treatment. However, it most often appears a few weeks after a lapse of inadequate arsphenamine

therapy. Moore<sup>9</sup> states that the average interval without treatment before the development of the neurorelapse is eight weeks. It is more apt to occur in patients treated entirely with arsenicals rather than by use of arsenicals and heavy metals combined.

The *onset of symptoms* of neurorelapse is often sudden, although it may be gradual. Headache may be the initial symptom. It is usually severe and may be accompanied by a convulsion, dizziness, nausea and vomiting. In severe cases, the patient may become stuporous and comatose. An accompanying edema of the optic discs may occasionally lead the physician to suspect that the patient has a tumor of the brain. This is particularly true if he fails to obtain a history of a recent inadequately treated early syphilis.

Because of the acute basilar meningitis, *cranial nerve palsies* are frequent. Any of the cranial nerves may become involved, but the eighth, seventh and second nerves are most frequently affected. Hemiplegia and aphasia may result from involvement of the cerebral cortex or as a result of a vascular endarteritis or thrombosis.

Neurorecurrence is prone to occur in patients in whom the blood serologic reactions have reverted to normal following the administration of comparatively little treatment. It is not uncommon for the blood serologic reactions to be negative or only weakly positive at the onset of symptoms. However, the spinal fluid shows a high cell count, increase in globulin, marked increase in total protein, a strongly positive serologic reaction, and usually a positive colloidal gold reaction of the paretic type. In a rare type of neurorecurrence the inflammatory process may be more or less localized and in such a case the spinal fluid may or may not be abnormal.

**Cases Illustrating Neurorecurrence.**—*Case 1.*—A colored man, aged twenty-six, came to the Clinic on March 4, 1937, complaining of inability to move the right side of the face, and right arm and right leg during the past twenty-four hours. He had had intermittent attacks of severe frontal head-

ache and soreness of the muscles of the posterior part of the neck for the past two months.

The day before admission he had experienced three attacks of numbness and twitching of the right arm, difficulty in speaking and increased salivation. These attacks were of short duration. On retiring he felt well but, at 5:30 a.m., he was awakened by a severe frontal headache. Shortly afterwards he observed that the whole right side of his body was paralyzed.

Late in 1935 he discovered that he had seropositive primary syphilis. He received continuous and regular antisyphilitic treatment for eight months. This consisted entirely of intravenous medication—probably neoarsphenamine. At the end of this time his blood serologic reactions were negative and he was told that he was cured. There was no examination of the spinal fluid and he was not advised to return for further treatment or observation. Approximately three months later he began to have intermittent frontal headache.

The patient was a well developed and well nourished Negro. He was mentally alert and, with the exception of a complete right-sided hemiplegia, he appeared to be in good condition. There was no paralysis of the ocular muscles and no impairment of hearing. Blood Wassermann and Kahn reactions were 4+. The spinal fluid showed: cell count 130, all lymphocytes, trace of globulin, 125 mg. per cent total protein, Wassermann 4+, and negative colloidal gold chloride reaction.

A diagnosis of neurorecurrence was made. It was felt that the hemiplegia was probably the result of a vascular lesion rather than a syphilitic involvement of cortical meninges and adjacent cerebral cortex. For this reason the initial anti-syphilitic treatment consisted of sodium iodide by mouth and biweekly intramuscular injections of a soluble bismuth.

Within slightly less than a month, the paralysis of the extremities had completely disappeared, but there was some residual facial paralysis. Headaches had disappeared and the patient insisted on leaving the hospital. Arsenical medication was begun with small doses in order to avoid a Herxheimer re-

action at the site of the suspected vascular involvement. Clinical improvement was rapid and progressive. Further treatment was intensive and consisted of alternating courses of arsphenamine and bismuth salicylate. After the initial course of twelve injections of arsphenamine, difficulty with phlebitis necessitated changing to mapharsen.

This patient is still under treatment. As an adjunct to standard treatment he has received fever therapy in an electric cabinet. Spinal fluid findings are still abnormal, but he is symptom-free and is continuing with regular and intensive antisyphilitic therapy. It is too soon to determine the ultimate outcome in this case; however, the prognosis should be guarded.

*Case II.*—A single woman, aged thirty-three, came to the Clinic on July 18, 1933, complaining of headache, nausea, vomiting, diplopia and blurring vision. In November, 1932, she developed a genital lesion which was followed by a generalized eruption and a sore throat. At this time the blood serologic reactions were positive. Before the onset of her present illness she had received approximately twenty intravenous and eight intramuscular injections. Four blood tests, including one taken a week before coming to the Clinic, were negative. Her physician had not examined her spinal fluid. Unfortunately the date of the last treatment was not ascertained. Approximately seven months after she had developed secondary syphilis she began to have severe, diffuse headaches which were most severe in the mornings. Nausea and vomiting had become troublesome symptoms, and four weeks after the onset of headache she developed diplopia, blurring of vision, and an impairment of speech.

The patient was a well developed young woman. She was, however, stuporous and answered questions poorly. There was a paralysis of the left external rectus muscle with a nystagmus to the left. The pupils were normal. The eye grounds showed hyperemic inflammatory vascular changes. There was a partial paralysis of the right facial nerve, an absence of the abdominal reflexes and a positive Babinski reflex on the

left side. There were mucous patches on the buccal mucosa, but there were no lesions on the skin or genitalia.

The blood Wassermann reaction was negative but the Kahn reaction was 3+. The spinal fluid was of a faint yellow color and contained 120 red cells and 250 white blood cells per cu. mm.; globulin was 2+, the total protein 110 mg. per cent, Wassermann 4+, and the colloidal gold chloride reaction 5-5-5-5-4-3-1-0-0-0 (paretic curve). It was thought that the color of the fluid and red blood cells were the result of an old subarachnoid hemorrhage.

A diagnosis of neurorecurrence was made and treatment was started with arsphenamine. Following four treatments she was greatly improved and returned home to continue intensive treatment by her private physician.

*Case III.*—A single man, aged twenty-eight, came to the Clinic on July 5, 1933, complaining of headache and a recent sudden onset of weakness of the right side of the body. In September, 1932, he had contracted syphilis. Six hours after he had been exposed to syphilis he received one injection of neoarsphenamine. However, he developed a primary lesion and within two months secondary syphilis appeared. At this time his blood serologic reactions were strongly positive. Anti-syphilitic treatment was begun and, after he had received ten injections of neoarsphenamine and five injections of bismuth, he voluntarily discontinued treatment. Eight weeks after he received the last treatment he began to have attacks of headache accompanied by a pain in the upper dorsal region. This pain radiated down each arm to the elbows. Six weeks later he began to have attacks of transitory incomplete right-sided hemiplegia. Between attacks he noticed that there was a residual weakness of the right upper and lower extremities.

The patient was a slender, well developed, alert, young man. The general physical examination showed normal findings except for a partial paralysis of the right arm and leg and a bilateral Babinski reflex. There were no cranial nerve palsies. Examination of the eyes showed a low grade inflam-

matory neuroretinitis. The blood Wassermann reaction was negative and the Kahn reaction was 1+. The spinal fluid findings were: cell count 410 (75 per cent lymphocytes and 25 per cent polymorphonuclear leukocytes), globulin 2+, total protein 150 mg. per cent, Wassermann reaction 3+, and the colloidal gold chloride reaction 5-5-5-5-5-4-3-1-0 (strong paretic curve).

Following six injections of arsphenamine, all symptoms with the exception of a slight residual weakness of the right arm had disappeared. The patient left the hospital to continue intensive antisyphilitic treatment with his family physician.

These three cases are examples of neurorecurrences. In each case the syphilitic infection was in the early stage of the disease. In the first case treatment had consisted entirely of arsenical medication, in Case II relatively little heavy metal had been given, and in Case III the patient voluntarily discontinued treatment after receiving only a few injections of neoarsphenamine and bismuth. In each case treatment was inadequate and, in two of the cases, the onset of symptoms appeared a few weeks after a lapse of treatment. It should be pointed out that, in Case II, the family physician had placed too much confidence in the blood serologic reactions and had erred in failing to examine the spinal fluid at the onset of symptoms. Likewise in Case I, the physician was more negligent when he discharged the patient as cured without having first examined the spinal fluid. It is a regrettable fact that, on the whole, medical men are averse to examination of the spinal fluid of patients who are receiving treatment for early syphilis and in patients with latent syphilis.

In the treatment of neurorecurrence, *arsphenamine therapy must be intensified*. The dosage must be increased and the courses prolonged. The interval between injections should be decreased. Courses of *heavy metals* should be given between the courses of arsenical medication. Treatment must be *regular, continuous and prolonged*. The *spinal fluid* should

be examined *every six months*. In resistant cases, *fever therapy*, preferably with malaria and in selected cases tryparsamide, should be used.

**Headache of Late Syphilis.**—In late syphilis of the central nervous system, headache is frequently a prominent and distressing symptom. It occurs most often in the meningo-vascular type of neurosyphilis, and may *precede* by months or years the appearance of the more familiar neurologic signs. The *intermittent* character of the headache and the frequent association of *nausea, vomiting* and *slight attacks of dizziness* (which are at times misinterpreted as visual disturbances), are responsible for the *erroneous diagnosis of migraine* which is frequently made in headache of late neurosyphilis. A *routine blood test* in cases of chronic intermittent headache, and the *examination of the spinal fluid* in all cases of headache for which no cause can be found, would in many cases reveal the true cause of the patient's illness and result in prompt relief from one of the most distressing and agonizing of symptoms.

Contrary to what might be expected, the *severity* of the headache does not always parallel the degree of abnormalities found in the spinal fluid. In most cases of late neurosyphilis in which headache is a prominent symptom, the spinal fluid is abnormal. However, in cases in which headache is due chiefly to syphilitic endarteritis or in cases of gumma of the brain, the spinal fluid may be normal. Likewise, a chronic syphilitic basilar meningitis may occasionally produce a dull stupefying frontal or occipital headache without the usual associated abnormalities in the spinal fluid.

**Cases Illustrating Common Types of Late Syphilitic Headache.**—*Case IV.*—A woman, aged thirty-five when she came to the Clinic in January, 1926, complained of headache and dizziness. For the past six months she had had recurrent attacks of severe occipital headache which were accompanied by dizziness and, at times, by nausea and vomiting. Occasionally there was a severe pain at the vertex of the scalp. The headache usually lasted at least twelve hours.

matory neuroretinitis. The blood Wassermann reaction was negative and the Kahn reaction was 1+. The spinal fluid findings were: cell count 410 (75 per cent lymphocytes and 25 per cent polymorphonuclear leukocytes), globulin 2+, total protein 150 mg. per cent, Wassermann reaction 3+, and the colloidal gold chloride reaction 5-5-5-5-5-4-3-1-0 (strong paretic curve).

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It should be emphasized that in cases of this kind *it is not uncommon for the spinal fluid to be normal*. Likewise, the blood serologic reactions may be negative or only weakly positive. A past history of a positive Wassermann and Kahn reaction, or of antisyphilitic therapy, is of great importance. In cases of this kind a *careful history* should be obtained.

*Case V.*—A woman, aged fifty-nine, came to the Clinic complaining of severe unilateral headache of five weeks' duration. The headache was intermittent and involved the right side of the head. Occasionally the headache was accompanied by pain over the right side of the face, dizziness and nausea. She had been told that her headache was caused by a sinus infection and was contemplating having an operation when she came to the Clinic.

Physical examination showed no abnormal signs. There were no ocular palsies. The blood Wassermann reaction was 2+ and the Kahn reaction 3+. Spinal fluid findings were: cell count 120 (lymphocytes), trace of globulin, total protein 50 mg. per cent, Wassermann 4+, and colloidal gold reaction negative.

The patient had never had a blood test and had no idea when she had contracted syphilis. She had been married twice. Her first husband had died of a malignancy. Her present husband denied having had a venereal disease and his serologic reactions were negative.

All symptoms disappeared promptly following the institution of antisyphilitic treatment. This patient is at present receiving regular and continuous treatment.

In this case the headache was atypical in that it was unilateral and roughly simulated a sinus headache. The high cell count in the spinal fluid indicated an active syphilitic meningitis.

*Case VI.*—A married man, aged thirty-seven, came to the Clinic on March 9, 1939. His chief complaint was severe, intermittent headache of three years' duration. He had been told

Physical examination showed no abnormalities and a provisional diagnosis of migraine was made by the physician who examined her first. The routine blood Wassermann and Kahn reactions were strongly positive. She did not submit to a lumbar puncture. She did not know when she had acquired syphilis. Following the administration of 13 injections of bismuth and 10 injections of neoarsphenamine she was entirely free of all her original symptoms. Treatment was interrupted because of an attack of appendicitis which necessitated an operation. She remained in good health for ten years, during which time she neglected to take further antisyphilitic treatment.

In 1936, the patient noticed that she was gradually becoming nervous, irritable, and had difficulty in going to sleep. She would awaken early in the morning with a severe occipital headache which at times was accompanied by nausea and vomiting. At first these attacks came once or twice a month, but recently they had gradually become more frequent and severe. Consequently she returned to the Clinic in 1938. At this time there were no abnormal neurologic signs. The blood Wassermann reaction was negative and the Kahn reaction was 1+. The spinal fluid findings were: no cells, no globulin, total protein 35 mg. per cent, colloidal gold reaction negative.

In view of her past history she was advised to resume antisyphilitic treatment. Treatment has consisted of potassium iodide by mouth and alternating courses of bismuth and neoarsphenamine. Treatment has been regular and continuous. The stupefying intermittent headache and all other symptoms promptly disappeared and the general health of this patient has steadily improved. Six months after antisyphilitic treatment was started this patient remarked, "I haven't felt so well in many years."

The headache which this patient complained of was caused by late neurosyphilis of the vascular type. *Headache, dizziness, irritability, insomnia* and *nausea* are prominent manifestations of *syphilitic cerebral endarteritis*. In all probability there was an associated chronic syphilitic basilar meningitis.

antisyphilitic treatment in a patient with a genital lesion *without first determining by a darkfield examination that the lesion is chancre*. The diagnosis of acute syphilis must be confirmed by laboratory findings and should never be based upon the clinical impression of the examining physician, regardless of his experience or professional standing.

*Gumma of the brain* is a rare manifestation of late syphilis which may cause a stupefying headache, accompanied by nausea, vomiting and a choking of the optic discs. The symptom complex produced by gumma of the brain is the result of intracranial pressure and is identical with that resulting from a neoplasm of the brain. With gumma of the brain, the spinal fluid and blood serologic reactions may be normal. Alpers<sup>10</sup> states that a clinical diagnosis of gumma cannot be made with certainty, that the treatment of suspected gumma of the brain should be surgical, and that antisyphilitic treatment should be withheld until the gumma has been removed.

**Summary.**—Headache is a common and distressing symptom which may be caused by many different and unrelated conditions. The discovery of the cause of headache may be a difficult and, at times, an impossible task; however, if the possibility of syphilis as an etiologic factor is considered in cases in which the cause of headache has not been determined, the solution of quite a few patients' difficulties will be reached.

Syphilis is a common disease and, since headache may be caused by a syphilitic meningitis or cerebral endarteritis, it behooves the physician to be "syphilis conscious." A thorough examination of a patient who complains of an intermittent, stupefying headache should include among other procedures a blood serologic reaction and an examination of the spinal fluid. In some cases of late neurosyphilis the serologic reaction and spinal fluid findings may be normal; however, these diagnostic procedures will result in the discovery of many cases of neurosyphilis which otherwise would not have been recognized.

Headache of syphilitic origin may occur during the early or late stages of the disease. In the early stages of syphilis, headache is usually caused by a syphilitic meningitis. Headache is not an uncommon but seldom a major symptom of un-

that his headaches were the result of a sinusitis. The headache was severe and occurred during the daytime, usually near noon, and would last four to five hours. Occasionally there were prodromal symptoms, consisting of tingling of the tongue and numbness of the hands. When the pain was intense there was slight blurring of vision, nausea and vomiting. Headache was relieved by vomiting.

Physical examination showed no abnormal findings. The eye grounds were normal. Blood Wasserman reaction was negative but the Kahn reaction was 2+. Spinal fluid findings were: cell count 48 (lymphocytes), trace of globulin, total protein 105 mg. per cent. Wassermann 4+, colloidal gold reaction 2-2-2-1-0-0-0-0-0-0.

At the age of twenty-seven, this patient had developed a penile lesion. The physician whom he consulted made a clinical diagnosis of primary syphilis but failed to confirm the diagnosis by a darkfield examination. The lesion disappeared after he had received four injections of neoarsphenamine. He had received no further antisyphilitic treatment, and it had not occurred to him that his present illness might be caused by syphilis. He had a routine blood test four years before the onset of his present illness and it was reported as negative. The patient has been receiving intensive antisyphilitic treatment from his family physician for the past eight months and in a recent letter he reported that he was free of symptoms, and that he expected to return soon for an examination of his spinal fluid. It may be advisable for this patient to take malarial treatment before continuing with standard antisyphilitic treatment.

In this case, headache which was the patient's chief complaint, was caused by late stage of the central nervous system. The spinal fluid findings were of the early type. The pleocytosis indicated the presence of a chronic meningitis.

This case is a good example of the late stage of syphilitic origin, and it is important to remember that there is no

## HEADACHE OF RENAL ORIGIN

R. H. McDONALD

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HEADACHE is a symptom which has no particular diagnostic significance in bilateral parenchymatous non-suppurative renal disease, but it is frequently present and is related to one or other of the numerous disturbances caused by the renal lesion. The *acute phase of renal disease* is usually part of a more widespread inflammatory lesion, and toxic absorption from other areas, as well as from an inflamed kidney, occurs. With *renal insufficiency*, there is an accumulation within the body of waste products which produce an irritation of the meningeal sensory nerves. Finally, the mechanical disturbances of cerebral circulation and intracranial pressure which occur with *increased blood pressure* may result in degrees of cephalalgia.

**Hemorrhagic Bright's Disease.**—In acute hemorrhagic Bright's disease (typically the sequel of a streptococcal infection elsewhere), there is frequently a marked febrile reaction. As in fever from other causes, there is frequently marked meningeal irritation from the absorption of toxic products of disturbed metabolic processes. Usually such headache is generalized. In severe cases, where marked elevation of blood pressure accompanies the renal lesion, severe throbbing headache may result. It may be well localized and apparently dependent upon local aberrations of blood flow and it may be increased by effort or by a dependent position of the head. Cerebral vascular changes may be aggravated by the presence of a hypochromic anemia, with consequent inanition of the brain, although in the initial stages of the disease anemia seldom advances to the stage where this occurs. At times in

acute renal disease, the process interferes with the power of the kidney to perform its function of ridding the body of wastes and maintaining a normal blood concentration of electrolytes. Azotemia under such circumstances causes meningeal irritation and varying degrees of cephalalgia, usually rather dull and generalized. With recovery from the febrile stage and return of renal function, the headache disappears.

In many instances the onset of hemorrhagic Bright's disease is insidious and patients are first seen when the process has been of long duration. In these *chronic active cases*, headache becomes an outstanding symptom and may be the major complaint. It will be accompanied by the other usual symptoms of general weakness, *anorexia*, *polyuria*, *nocturia*, and perhaps *edema* of the dependent parts. A low grade toxemia is undoubtedly a factor in the production of the headache, but usually the accompanying elevation of pressure is the chief factor. Again the disturbance of cerebral circulation is aggravated by the anemia which is almost always present. The headache is usually of a generalized character and lacks the localization of the commoner forms of reflex headache. Occasionally, in chronic Bright's disease, it is possible that the retinal inflammation which occurs is in itself a cause of headache of reflex origin.

With the onset of *uremia* in terminal Bright's disease, headache becomes a very frequent and troublesome symptom. It may occur in any part of the head, often frontal or occipital; or it may be hemicranial, thus simulating migraine. This is especially so since it is frequently accompanied by nausea and vomiting, but it lacks the clear-cut character and periodicity of the migraine attack. As a rule, headache in the presence of uremia is not severe in contrast to that observed in the hypertensive encephalopathy to be discussed. It has been argued that headache is not a true symptom of uremia, but it has been noted repeatedly that patients who have not had headache previously do have it as an accompaniment of the abnormal increase of non-protein nitrogen in the blood which is significant of the uremic state.

**Hypertensive Encephalopathies.**—Headache is a symptom from which almost all patients with *essential hypertension* suffer at times, and frequently it is an initial symptom. It is still a question whether the genesis of primary vascular disease of this type is renal or extrarenal. Recent researches have suggested that interference with renal circulation may produce a substance which, in the presence of the adrenal gland, causes primary hypertension in contrast to the commonly accepted neurogenic theory. At any rate, the patient with essential hypertension displays many of the symptoms associated with primary renal disease, especially the increased blood pressure, and eventually presents a well recognized type of renal lesion which may go on to renal insufficiency. It is a common finding that patients with essential hypertension have suffered since childhood from headache suggestive of the migraine type. Such a history apparently indicates some inherent instability of the autonomic vasomotor nervous system which later renders these patients more susceptible to essential hypertension.

A special type of headache is that described under the term *hypertensive encephalopathy*. It may be preceded by visual or auditory *aurae*, and accompanied by *nausea*, *vomiting* and transient *paralysis* and *aphoria*, and at times with *epileptiform convulsions*. The headache is frequently intense, sharply localized with definite onset and culmination, and strongly suggestive of localized cortical vascular spasm. It is probably the most dramatic complication of renal disease.

*Renal insufficiency* in essential hypertension may be accompanied by uremic headache, but the vast majority of headaches of patients with essential hypertension are not due to uremia, as is indicated by the normal blood findings.

The *sequelae* of essential hypertension may be the cause of severe headache. The onset of a *cerebral hemorrhage* may be marked by an uncontrollable localized pain in the head, which apparently is the result of meningeal irritation and cerebral damage. *Cerebral thrombosis* may produce similar symptoms. Occasionally, in hypertensive encephalopathy, *edema*

*of the brain* develops and the intracranial pressure is increased to such an extent that choked disc appears. In such cases the clinical picture of violent headache, nausea, vomiting, convulsions and marked elevation of cerebrospinal fluid pressure appears as in any other space-filling lesion of the cranium.

**Treatment.**—Recognition of the *renal origin* of the symptom is dependent upon the history of antecedent renal disease or hypertension, urinary examination, renal function and blood chemistry studies. Apart from the use of *sedatives* and *analgesic drugs* for symptomatic relief or the judicious use of *lumbar puncture* in a few cases, treatment must be directed toward the care of the *underlying renal condition*.

## MULTIPLE MYELOMA, OR MYELOMATOSIS

RUSSELL L. HADEN AND JOHN M. RUMSEY

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IN 1850 William McIntyre<sup>1</sup> first reported a case of multiple myeloma under the title: "Case of Mollities and Fragilitas Ossium." This patient had spontaneous fractures of two ribs and neuritic pains. It was in this case also that Bence-Jones first found the protein now known by his name.<sup>1</sup> Bence-Jones pointed out that this substance, after precipitation, redissolved on heating and precipitated out again on cooling.

**Pathology.**—A myeloma is a tumor of the marrow. This term was first used by Rustizky<sup>1</sup> in reporting the postmortem study of a patient with multiple tumors of the bones of the trunk. The term "multiple myeloma" is unfortunate and misleading for the cases reported in this paper since it indicates the presence of discrete tumors arising from the bone marrow. The disease may manifest itself as single or multiple tumors, as a generalized hyperplasia of the marrow alone, or as a generalized hyperplasia with discrete tumor formation. For this reason the designation *myelomatosis* is preferable to multiple myeloma since it includes all cases with varying manifestations.

Myelomatosis is related to myeloid leukemia in that it is a disease of the *bone marrow* and belongs in the *malignant* group of tumors. It is a relatively uncommon disease. Atkinson,<sup>2</sup> in 1937, could find only 637 reported cases. It certainly occurs more frequently than is usually thought, however, as many cases are undiagnosed. It is our experience that the ratio of myelomatosis to myelocytic leukemia is about 1:5.

*Myelomatosis differs in a number of ways from myeloid leukemia:* The myeloid hyperplasia in myelomatosis is usually

due to overgrowth of plasma cells. These cells, which occur so abundantly in the bone marrow, seldom are found in the blood stream. Likewise, if the myelomatosis is due to hyperplasia of other elements of the marrow, there is no overflow of the abnormal cells into the circulation. The hyperplasia of plasma or other cells is accompanied by a demineralization of bones, so there is some element of the invasiveness characteristic of malignant growths. In myelocytic leukemia there is usually the appearance of immature cells of the myeloid series in the circulating blood, although this is not necessary. It is exceedingly uncommon, however, to have any evidence of demineralization or invasiveness of bone. Plasma cell leukemia has been reported, but it is very rare. Myelomatosis is thus best thought of as a malignant disease of the bone marrow in which the framework of the bone is gradually destroyed, usually by the generalized overgrowth of plasma cells without the appearance of these cells in the blood. With myeloid leukemia, in contrast, there is usually an overflow of the immature cells of the myeloid series into the blood stream and no demineralization or destruction of bone resulting from the hyperplastic marrow. In myeloid leukemia also, there is overgrowth of all myeloid cells; in myelomatosis a single cell type is usually hyperplastic. At one end of the myelomatosis scale there is the single tumor of bone marrow origin; at the other, the generalized hyperplasia without tumor formation. In between these two extremes are all combinations of the two pathologic processes.

**Symptoms.**—Myelomatosis gives no symptoms early, since no pain is caused by the hyperplasia of marrow. Thus the skull may be riddled with small tumors, shown as "*punched out*" areas in the roentgenograms, without pain or tenderness on palpation. With the decalcification and softening of the bony framework which always occurs with involvement of the vertebrae and ribs, the vertebrae are compressed with the production of neuritic pain, and spontaneous fractures of the ribs often occur. *Neuritic pain*, especially in the back, is thus the one most characteristic and constant symptom of the disease.

This may often be precipitated by slight trauma. In advanced cases, simply turning over in bed may fracture a rib. The *nerve involvement* may even lead to *paralysis* and *paresthesia*. It is apparent that a movement is likely to bring on or accentuate the pain.

The second characteristic symptom in myelomatosis is weakness, due in part to the toxemia incident to the disease but resulting largely from the anemia which is almost an invariable symptom when the condition is well developed. The disease is pretty well limited to the bones normally containing red marrow in which erythropoiesis and leukopoiesis are most active. With the overgrowth of plasma cells or other cells of the myeloid series, the red cells are crowded out so that erythropoiesis is inhibited. A second factor in the production of the anemia is the toxemia characteristic of malignant disease, which depresses red cell formation even in normal marrow. A third factor is the frequent kidney involvement which has a depressant action similar to malignancy. The anemia is usually normocytic and hypochromic, but may be a macrocytic one suggesting pernicious anemia. In some cases the *anemia* may be the most marked symptom of the disease as nerve involvement may never occur or occur only very late in the course of the disease.

**Diagnosis.**—The physical examination in myelomatosis usually shows little unless there is an evident anemia. Sometimes there is pain on compressing the ribs or tenderness on pressure over the dorsal vertebrae.

The diagnosis is usually made by *roentgen examination* or the finding of Bence-Jones protein in the urine. The skull, vertebral column and ribs should always be *x-rayed*. The skull usually shows the "punched out" areas if these are to be found anywhere. Decalcification is best seen in the vertebrae and compression is usually evident in advanced cases. The ribs may show decalcification, "punched out" areas and spontaneous fracture.

The *Bence-Jones protein* is a proteose which precipitates as the acidified urine is heated to 56° C. With further heating

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The *Bence-Jones protein* is a proteose which precipitates as the acidified urine is heated to 56° C. With further heating

the precipitate redissolves only to appear again as the urine cools. This substance may be found in the blood also. We have demonstrated Bence-Jones protein only in plasma cell myelomatosis, so it is probable that it arises from plasma cells only. The sedimentation rate is usually elevated; the total blood proteins are often increased due to a greater than normal amount of globulin; the serum calcium may be increased; auto-agglutination of the red cells may occur.

Since myelomatosis is usually due to an overgrowth of plasma cells, the absolute diagnosis is best made by the demonstration of a *preponderance of plasma cells in the marrow*, obtained by aspiration of marrow from the sternum. Even if the localized tumors indicated by the "punched out" areas in the roentgenogram are present, the sternal puncture will show the plasma cells. It is not necessary to biopsy a localized lesion. Likewise, a *sternal puncture* may make an absolute diagnosis of myelomatosis even if the roentgenograms are not diagnostic. The sternal puncture is made with a large needle at the level of the third interspace. Only a small bit of marrow is aspirated. Films are made and stained with Wright's stain.

The *kidney involvement* often demonstrable late in the disease is most important. Usually the kidney function is low and the blood urea elevated. The kidney disease may accentuate the anemia. Bell<sup>3</sup> thinks the renal involvement is due to the accumulation of the Bence-Jones protein in the tubules, capillaries and glomeruli. We have seen kidney disease only in plasma cell myelomatosis.

#### ILLUSTRATIVE CASES

The following cases have been selected to illustrate characteristic clinical, radiographic and pathologic findings in myelomatosis:

**Case I. Plasma Cell Myelomatosis with Typical Skeletal Pain and Characteristic "Punched Out" Areas in the Roentgenogram.**—Five months ago this fifty-two-year-old man developed pain in the lower back which radiated to

the abdomen. The pain was made worse by bending or lifting, and had been constant and progressive. The weight loss was 12 pounds in five months. The only important physical findings were tenderness over the fourth rib on the right and limitation of motion of the back.

The roentgen examination of the skull and ribs showed many areas of bone destruction due to tumor formation (Fig.

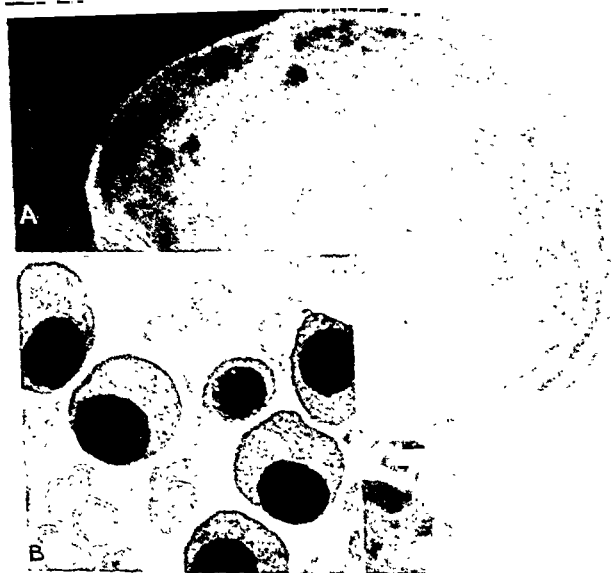


Fig. 38.—A, Radiograph of skull of Case I showing typical "punched out" areas characteristic of multiple myeloma. B, Photomicrograph of marrow obtained by puncture of the sternum. All the white cells are plasma cells.

38, A). Urinalysis was negative except for a trace of albumin. The blood count showed: erythrocytes, 4,380,000; leukocytes, 3,250; hemoglobin, 81 per cent; volume index, 1.01; and color index, 0.92. The sedimentation rate was 1.45 mm. per minute (normal 0.45 mm. per min.); calcium, 10.4 mg.; phosphorus, 3.1 mg.; and total serum proteins, 8.7 per cent, with albumin 4.9 per cent and globulin 3.8 per cent. Bence-Jones protein was absent in both blood and urine. The marrow puncture

showed a large proportion of plasma cells typical of myelomatosis (Fig. 38, *B*).

*Comment:* This is an unusually typical case of myelomatosis due to plasma cell overgrowth. The patient first consulted an orthopedic surgeon on account of low back pain. The roentgenograms were characteristic and the marrow puncture revealed only plasma cells. Bence-Jones protein could not be demonstrated.

**Case II. Plasma Cell Myelomatosis with Marked Anemia as the Presenting Symptom and Little Skeletal Pain.**—This man noticed weakness five months before he was



Fig. 39.—*A*, Radiograph of skull of Case II who died of anemia and renal involvement secondary to myelomatosis. Notice the relatively slight changes in the skull; the typical "punched out" areas are absent. *B*, Photomicrograph of marrow obtained by sternal puncture showing the plasma cell overgrowth.

seen. Three months after the onset of weakness he was first seen by a physician. A macrocytic anemia was discovered and became progressively more marked in spite of therapy. There

were no positive physical findings. The roentgen examination of the chest and spine was negative and only indefinite areas of rarefaction were noted in the skull (Fig. 39, A). The blood examination showed 1,340,000 erythrocytes and 2,450 leukocytes; there was marked auto-agglutination of the red cells. The hemoglobin was 37 per cent; the volume index, 1.6; the color index, 1.37; the serum calcium, 8.3 mg., and the blood urea, 147 mg. Bence-Jones protein was not found in the blood but was detected in the urine. The total serum proteins were 10.9 gm. per 100 cc., the albumin being 2.7 gm. and the globulin, 8.2 gm. The marrow puncture revealed only plasma cells (Fig. 39, B). There was a positive Takata-Ara test. This patient died three weeks later of uremia.

*Comment.*—This patient had remarkably little neuritic or other skeletal pain. The anemia occurred early and confined him to bed. This fact may explain the absence of vertebral compression and nerve root pain. The anemia and kidney involvements were extreme. He showed the characteristic auto-agglutination of red cells and elevated blood proteins.

**Case III. Generalized Decalcification of Vertebrae Due to Overgrowth of Myeloid Cells Other Than Plasma Cells.**—This sixty-nine-year-old woman began to have pain in the abdomen and back about two years before admission. The pain at first was intermittent, but had been constant during the last five weeks. She had weakness and nausea, with marked accentuation of the pain in the chest, back and abdomen on exertion, and had lost 30 pounds in weight.

The positive physical findings were a red tongue, limited expansion of the chest, soft mitral and aortic systolic murmurs with some cardiac enlargement, some hyperesthesia of the skin over the back, chest and abdomen, absence of the Achilles reflexes, and some limitation of motion of the spine.

The roentgenogram of the spine showed marked osteoporosis and a compression deformity of several vertebrae (Fig. 40). The blood count showed 4,160,000 red cells, 5.50 white cells, 78 per cent hemoglobin, a volume index of 0.99,

and a color index of 0.94. Bence-Jones protein was not found in either blood or urine. The marrow puncture showed a very hyperplastic bone marrow but only a few plasma cells. The patient has improved with irradiation.

*Comment:* This patient had such a generalized demineralization she was considered an example of senile atrophy of



Fig. 40.—Radiograph of thoracic spine of patient with myelomatosis showing the collapse of several vertebrae due to hyperplasia of marrow and decalcification of bone.

bone. The marrow was very hyperplastic, however, showing that this was the cause for the loss of bony framework. The overgrowth was not due to plasma cells and was improved by irradiation therapy.

**Case IV. Generalized Decalcification Due to Hyperplasia of Bone Marrow and Localized Tumors of Myeloid Origin.**—This sixty-year-old, obese widow two and a half years prior to her first admission to the Clinic developed pain in the tips of the fingers with swelling of the fingers and clubbing. There was pain in the legs and chest. She had been bedridden for six months. During the last three months she

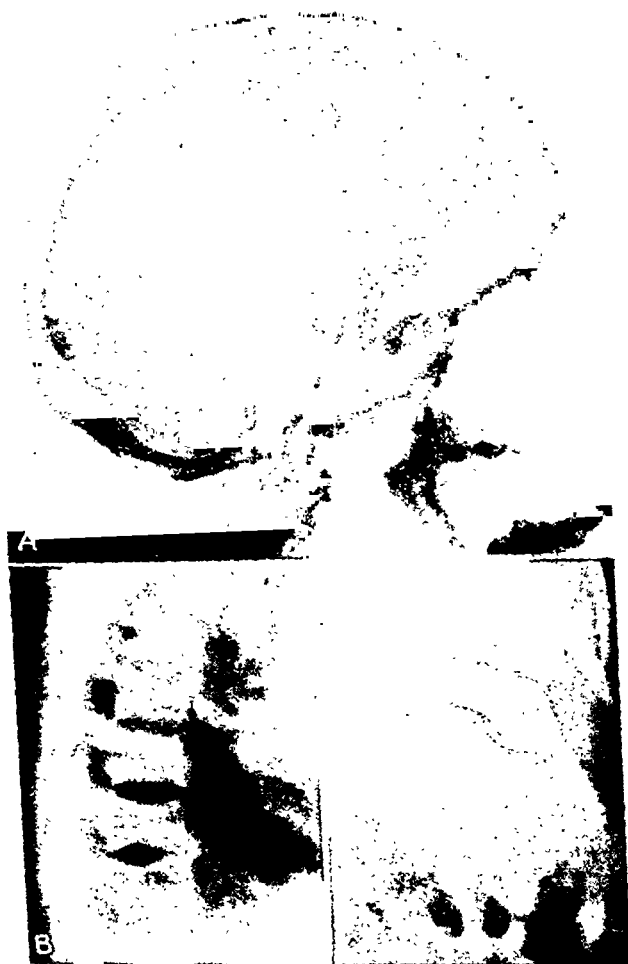


Fig. 41.—Radiograph of Case IV. The myelomatosis is due to hyperplasia of marrow cells other than plasma cells. A, Skull showing a few decalcified areas. B, Thoracic spine showing collapsed vertebrae due to softening. C, Rib showing a bulbous enlargement.

had had localized epigastric pain. There was marked tenderness over the ribs and the back, and she complained bitterly of pain on motion.

The roentgenograms showed renal stones on the right,

marked destruction in the right ilium, many demineralized areas in the skull and marked destruction and demineralization of the spine and the ribs (Figs. 41, *A, B, C*). The blood count showed erythrocytes, 4,050,000; hemoglobin, 71 per cent; volume index, 0.94; and color index, 0.88. The leukocyte count was 5,900 and the differential count normal. The urine showed albumin and pus cells; the blood urea was 81 mg. on one occasion and 63 mg. on another; the urea clearance was 21 per cent in the first hour and 31 per cent in the second. Bence-Jones protein was not found in blood or urine. The blood calcium was 8.0, 9.5 and 8.5 mg., and blood phosphorus, 2.4 and 2.8 mg. Calcium balance studies were within normal limits. The serum proteins were 5.7 per cent, 6.1 per cent and 4.4 per cent. Marrow studies showed hyperplastic marrow not of the typical plasma cell type. The patient received roentgen therapy to the spine and had very violent reaction. She has been followed for one year, and reports that she feels better but there is no objective evidence of improvement.

*Comment.*—This patient also had the type of hyperplasia similar to myeloid leukemia and seemed to respond to irradiation. The localized tumors, the absence of leukocytosis and abnormal cells in the circulation and the bone destruction excluded leukemia.

#### DISCUSSION

Twenty-two cases of myelomatosis have been analyzed in this group. The average age was fifty-eight years, the youngest patient being thirty years old. Sixteen of the patients were men, six women. In twenty patients the presenting symptom was *pain*, which was almost always in the back, chest, or abdomen. Two complained only of weakness due to extreme anemia. Pathologic fractures often occurred late in the course of the disease. The physical examination was not significant.

The most common roentgen finding was demineralization of the spine, often with collapse or compression of vertebrae. Changes in the ribs were common. Roentgenograms of the skull were taken in eleven cases. Marrow puncture was done

in sixteen cases and plasma cell hyperplasia was found in nine. In three cases, proved by marrow puncture, no abnormality was found; in eight, discrete "punched out" areas of decalcification were found. There is no definite relation of the type of myeloma to the radiographic findings, although the discrete areas of decalcification are more common with plasma cell myelomatosis.

*Anemia* was present in most cases. The lowest red cell count was 1,300,000. The leukocytes showed no characteristic change. The *sedimentation rate* was often elevated. Excessive rouleaux formation was usually evident.

The relation of *Bence-Jones protein* to myelomatosis is important. This has been found only when the disease is due to the overgrowth of plasma cells. Tests for Bence-Jones protein have been negative in blood and urine in seven cases due to other types of cells than plasma cell myelomatosis. In several instances Bence-Jones protein was found in the blood and in most cases in the urine. Even in cases due to plasma cell overgrowth, Bence-Jones protein may be absent. The blood proteins were determined in fifteen cases and in nine were increased. The increase was entirely in the globulin fraction. In eight of nine cases with hyperproteinemia a plasma cell myelomatosis was proved by marrow puncture.

In six cases the *blood urea* was markedly elevated; these also were all instances of plasma cell myelomatosis. It seems evident that the *renal involvement* is a manifestation of the presence of Bence-Jones protein, as in five of the six cases this protein was found present. It might well be that the renal failure was due to plugging of the glomeruli and tubules with the Bence-Jones protein as suggested by Bell.<sup>3</sup>

The cases of plasma cell myelomatosis run a more malignant course than when due to other types of cells and *do not respond to irradiation*.

#### SUMMARY AND CONCLUSIONS

Myelomatosis or multiple myeloma is not an uncommon disease.

Its presence should be suspected with generalized skeletal pain, especially if there is evidence of nerve root pressure, or if there is a coincident anemia.

If suspected, roentgenograms of the skull, vertebrae and ribs should be taken, the urine examined for Bence-Jones protein, and a marrow puncture made.

Most cases of myelomatosis are due to a hyperplasia of plasma cells which are easily identified in sternal marrow preparations.

Often the roentgenograms show no characteristic "punched out" areas. There may be only generalized demineralization, or relatively little change.

The finding of Bence-Jones protein is almost diagnostic of plasma cell myelomatosis, but the absence of this protein does not exclude any type of myelomatosis.

The treatment of plasma cell myelomatosis is very unsatisfactory as it does not respond to irradiation.

In other types of myelomatosis irradiation should be tried.

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## GASTRO-INTESTINAL MANIFESTATIONS OF CARDIOVASCULAR DISEASE

A. CARLTON ERNSTENE

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SYMPTOMS referable to the gastro-intestinal tract frequently are present in patients with cardiovascular disease and at times are of such prominence that they dominate the clinical picture. Since their misinterpretation may lead to serious errors in diagnosis, proper understanding of the mechanism of their production is of considerable importance. It will be the purpose of this communication to review the pathogenesis of the gastro-intestinal manifestations of cardiovascular disease and to point out the manner in which the correct evaluation of accompanying symptoms and signs will assist in differential diagnosis.

**Dysphagia.**—Dysphagia is an unusual symptom of cardiovascular disease, but occasionally it occurs as the result of pressure upon the esophagus by an *aortic aneurysm* or a *greatly enlarged left auricle*. Less frequently it is produced by pressure from a large *pericardial effusion*.

**Aortic Aneurysm.**—The esophagus is situated in close anatomic relationship to both the aortic arch and the descending aorta, and an aneurysm in either of these portions may exert considerable pressure upon it. Recognition of the cause of the resulting dysphagia is seldom difficult.

Aneurysms of the *aortic arch* may be accompanied by inequality of the pupils, venous congestion of the head and neck, a tracheal tug, dyspnea, disturbances in phonation, and inequality of the radial pulse wave and brachial blood pressure in the two arms. Aneurysms of the *descending aorta* frequently cause severe pain from pressure upon the spine and

nerve roots, and at times they may be responsible for cough and expectoration due to pressure upon the left main bronchus.

*Roentgen examination* of the chest establishes the diagnosis, but it is to be remembered that in ordinary anteroposterior films an aneurysm of the descending aorta may be completely concealed by the cardiac shadow. Radiologic study of the heart therefore should always include a film taken in the *right oblique* diameter as well as *fluoroscopic* examination, and in all individuals in whom dysphagia is present, studies of the esophagus should be made after the administration of thin barium paste.

*Enlargement of Left Auricle.*—In patients with mitral valve disease (stenosis, insufficiency, or both) the left auricle is the first chamber of the heart to become enlarged. This enlargement alone may cause very little change in the size of the heart as seen in the anteroposterior diameter, although there usually is an associated prominence of the pulmonary conus. The posterior surface of the heart is comprised principally of the left auricle, even moderate enlargement of which results in projection of the auricle into the retrocardiac space. The anterior wall of the esophagus normally is in contact with the posterior surface of the heart. Enlargement of the left auricle, therefore, causes *displacement backward* and occasionally rather sharp *angulation of the esophagus*.

If the auricular enlargement is extensive, the pressure exerted upon the esophagus may result in marked dysphagia, as illustrated in the following case report:

*Case I.*—The patient, a white married woman aged fifty-four years, was admitted to the Clinic on January 6, 1933, because of dyspnea on exertion, difficulty in swallowing, and prominence of the veins of the neck and upper chest. The past medical history was irrelevant except for pneumonia at the age of nineteen years, at which time the patient had been ill for three months. In March 1932, fatigability and dyspnea on walking rapidly were first noted. These symptoms increased gradually in severity, and after two months a persis-

tent, slightly productive cough and edema of the ankles developed. Approximately three months before her admission to the Clinic, the patient noted the onset of difficulty in swallowing liquids. Solid food caused no trouble, but every attempt to take liquid resulted in at least partial regurgitation, either immediately or within a few minutes. One month after the appearance of dysphagia, the veins over the neck and chest became prominent and this had increased progressively.

Physical examination revealed a poorly nourished individual who experienced definite dyspnea while at rest. The lips and nail beds were cyanotic. The veins in both sides of the neck, both temporal regions, the anterior wall of the chest, and in the arms were tortuous and engorged. When the patient coughed, a number of small tortuous veins also became visible over the upper back. The heart was considerably enlarged to percussion; its rhythm was regular and the rate 120 beats per minute. A harsh systolic murmur was heard over the apex, but no diastolic element could be made out. The arterial blood pressure was 122 mm. systolic and 90 mm. diastolic and was the same in both arms. The percussion note was impaired over the base of the right lung and the breath sounds were diminished over this area. A few medium moist râles were heard over the base of both lungs. The liver extended 6 cm. below the costal margin in the midclavicular line and was moderately tender. Slight edema was present over both lower legs. Urinalysis and blood counts revealed nothing of significance. The Wassermann and Kahn reactions of the blood were *negative*.

An electrocardiogram showed auricular flutter with 2:1 block. Roentgenograms of the chest in the anteroposterior diameter revealed enlargement of the heart with calcific deposits in the pericardium. Films taken in the oblique diameter after the administration of barium paste by mouth showed obstruction of the esophagus due to pressure from an enlarged left auricle. Fluoroscopic examination revealed greatly diminished cardiac pulsations.

It is of considerable interest that, with absolute *rest in bed*

and the administration of *digitalis*, the patient's dysphagia disappeared entirely within one week.

**Anorexia, Nausea, and Vomiting.**—*Congestive Heart Failure.*—Anorexia is a common symptom in patients who have slight or moderate congestive heart failure, and in individuals with advanced failure there often is persistent nausea and repeated vomiting. In addition, many patients with congestive failure complain severely of flatulence. At times, these symptoms may be of sufficient prominence and so far out of proportion to such symptoms as dyspnea and cough that a diagnosis of some form of primary gastro-intestinal disease is suggested.

The symptoms are due to passive congestion of the gastric and intestinal mucosa and of the liver. Careful physical examination usually leads to proper interpretation of the patient's complaints. The heart is usually enlarged and its rhythm frequently is irregular. There generally is evidence of more or less extensive passive congestion of the lungs. The jugular veins are engorged and remain distended even when the patient is propped up in bed; the liver is enlarged and tender, and there is a variable degree of edema of the legs and over the lower back.

*Overdigitalization.*—Not infrequently a patient with congestive heart failure is first seen only after he has been under the care of another physician for some time. The patient may or may not know what medication he has been receiving, and the question arises whether the anorexia, nausea, and vomiting have resulted from overdosage with *digitalis*.

Fortunately, there are a number of points in the history and physical examination that usually enable one to make an accurate decision: In the first place, a description by the patient of the medicines he has taken and the dosages may be helpful. Secondly, if the patient has received sufficient *digitalis* to produce toxic symptoms he usually will report that there was decided improvement in the symptoms of myocardial failure after he began to take medicine and before anorexia or nausea and vomiting developed. If *auricular fibrillation*

is present and the ventricular rate is very rapid, one may safely conclude that the patient has not had too much digitalis, while the same arrhythmia with a ventricular rate of 60 or less suggests that large amounts of digitalis have been given. Frequent *premature beats* and especially *bigeminal rhythm* due to regularly recurring premature beats also increase the probability of digitalis overdosage.

In general, however, it will be found that in the individual who presents objective evidence of congestive heart failure, anorexia, or nausea and vomiting are the result of heart failure rather than digitalis intoxication. Under such circumstances the administration of *more digitalis* often results in prompt and complete relief from the gastro-intestinal symptoms.

*Coronary Disease.*—A sensation of distention or gas in the upper abdomen is a not infrequent complaint of individuals with coronary artery sclerosis, and occasionally repeated attacks of nausea and vomiting constitute one of the chief symptoms of the disease. Symptoms of this kind often cause the patient to diagnose his condition as "indigestion," but careful questioning and thorough physical examination usually reveal things in their proper light. In all but the exceptional case, a history of a *relationship* between the *appearance of symptoms* and *exertion* or *emotional upsets* will be present. Many patients will have observed that although even moderate activity soon after eating will cause symptoms, all discomfort can be avoided by limiting the size of the meal and by resting after eating. Furthermore, although there may be no actual pain in the substernal area during the time that symptoms are present, there almost always is at least a sensation of fullness, pressure, or gas in this location. Rest usually affords prompt relief from the symptoms, and vomiting, when it occurs, has a similar effect. Nitroglycerine also has a specific effect. On examination, the heart may or may not be enlarged, and its rhythm usually is regular. The arterial blood pressure frequently is elevated, and electrocardiograms often reveal evidence of coronary artery disease.

The following case report illustrates the manner in which *vomiting* may comprise an important part of the symptomatology of coronary artery disease.

*Case II.*—A white man, a musician aged sixty-eight years, was first seen on December 19, 1935, because of attacks of severe pain or pressure in the upper substernal area accompanied at times by forceful, almost projectile vomiting without preceding nausea. The first seizure had occurred one month earlier, and four of the five attacks that had been experienced had been brought on by exertion. In two attacks relief had been obtained by resting for a few minutes, but in the other three the pain had persisted until the sudden onset of vomiting about thirty minutes later. All seizures had been accompanied by moderate dyspnea. There had been no radiation of the pain from its upper retrosternal location.

Physical examination revealed a well developed, well nourished, anxious individual. The pupils were equal, regular, and reacted normally. The heart was not enlarged, and its rate and rhythm were normal. There were no murmurs. The peripheral arteries showed advanced diffuse sclerosis, and the blood pressure was 192 mm. systolic and 104 mm. diastolic. The lungs were clear on percussion and auscultation. Abdominal examination revealed no areas of tenderness and no palpable masses or solid organs.

The three conventional leads of the electrocardiogram showed no evidence of myocardial damage but, in precordial leads, the T waves were upright (old technic). Roentgen examination of the thorax revealed no evidence of pathologic change in the heart, aorta, or lungs. Roentgen examination of the gastro-intestinal tract also gave normal findings. Examination of the gastric contents after the administration of an Ewald meal showed normal concentrations of free and total acid. It was concluded, therefore, that the vomiting was due directly to coronary artery disease.

In spite of medication and a prolonged period of rest in bed with subsequent limitation of activity, the attacks of

pain continued to occur with increasing frequency, and developed more and more often while the patient was at rest. Many nocturnal seizures were experienced. Nitroglycerine never failed to give relief within a few minutes, but if for some reason nitroglycerine was not taken, almost explosive vomiting usually occurred within one-half hour and brought the attack to an end. The patient died on May 15, 1936, two hours after the onset of symptoms of acute coronary occlusion.

Nausea and vomiting often develop soon after the onset of acute coronary artery occlusion. Pain, however, is the outstanding symptom, and the differentiation between coronary occlusion and upper abdominal disease will be discussed from this viewpoint later.

**Jaundice.**—The bilirubin content of the blood is increased in practically all cases of *congestive heart failure*, and occasionally this increase is sufficient to produce visible jaundice. Icterus, when it occurs, is the result of two factors: The first of these is depression of the excretory function of the liver due to the anoxemia which results from passive congestion. The second is increased production of bilirubin as evidenced by its increased concentration in the blood and its increased excretion as urobilin in the stools and urine.

*Passive congestion of the liver* due to causes other than myocardial failure may also result in the appearance of icterus. *Extensive pericardial effusion*, for example, is accompanied by increased peripheral venous pressure, congestion of the viscera, and occasionally by jaundice.

When jaundice develops quickly in patients with congestive heart failure, or rapidly becomes more intense after having been present for some time, the change is usually due to *pulmonary infarction*. Infarction of the lung causes a sudden increase in the degree of anoxemia of the liver and reduces the already impaired excretory function of the hepatic cells. In many instances, the increased anoxemia causes actual necrosis of the liver cells in the center of the lobules.

The following case report illustrates the occurrence of jaundice in congestive heart failure with rapid intensification due to pulmonary infarction:

*Case III.*—The patient was a white man, forty-six years of age, who had had chronic cough and dyspnea on exertion for ten years. During the week before admission to the hospital these symptoms had increased and edema of the legs had been present. On physical examination, there was orthopnea, moderate cyanosis, and slight jaundice. The heart was enlarged, with systolic and diastolic murmurs at the apex. Auricular fibrillation was present. There were signs of congestion at the base of both lungs and of consolidation in the left mid-chest posteriorly. The liver extended almost to the level of the umbilicus, and there was edema of the legs and over the lower back.

During the first two days in the hospital, the jaundice increased greatly. Then for twelve days it gradually diminished as the patient's general condition improved. On the fourteenth day, however, there was an abrupt increase in dyspnea and cyanosis, and on the following day the jaundice was noted to be much more intense. There had been no cough, pain in the chest, or hemoptysis, and examination of the chest revealed no significant changes in the physical findings. The patient became comatose and died two days later. During the entire period of observation bilirubin had been present in the urine, but the stools had been of normal color.

Necropsy confirmed the diagnosis of rheumatic heart disease with mitral stenosis. The liver was enlarged and congested and showed necrosis of the central cells of the lobules in microscopic sections. The major portion of the cavity of the left auricle was occupied by a large, grayish-red, friable thrombus, and the lumen of the right inferior pulmonary vein was occluded by an attached thrombus which extended peripherally for a considerable distance along its tributaries. The lower lobe of the right lung was completely infarcted; it was deep red in color and of a firm, rubbery consistency throughout. Scattered through the rest of the lungs were many areas of thrombotic infarction, ranging from a few millimeters to 5 cm. or more in diameter. There were no areas of pneumonia.

Jaundice occasionally develops within the first two or three

days after the occurrence of *acute coronary occlusion*. Usually the icterus is of only slight degree but, at times, it becomes quite deep. The liver is generally enlarged and tender, and in all probability the development of jaundice is to be explained as a result of anoxemia of the hepatic cells.

**Abdominal Pain.—Congestive Heart Failure.**—A number of cardiovascular conditions may cause abdominal pain. Patients with advanced congestive heart failure often complain of discomfort or actual pain in the epigastrium and right upper quadrant of the abdomen due to the presence of an enlarged, congested liver. Recognition of the cause of the symptoms is a simple matter under such circumstances, and in favorable cases the institution of proper treatment results in prompt relief.

**Angina Pectoris.**—Although the pain of angina pectoris is typically retrosternal in location, it may occasionally be situated in the epigastrium.

In general, the *differentiation* of pain of this kind from that due to *abdominal disease* is not difficult. The relationship of the pain of angina pectoris to *exertion* and its prompt subsidence with *rest* is of fundamental importance. Furthermore, although the pain may not spread beyond its epigastric location if the patient becomes inactive with the first appearance of discomfort, it is much more common to have some radiation to the retrosternal area or at least an accompanying sensation of fullness, pressure, or tightness in this region. Physical examination of the patient with angina pectoris may reveal nothing of diagnostic significance, and the electrocardiogram may also fail to help. The ultimate diagnosis, therefore, must often be based upon a careful analysis of the patient's symptoms.

**Coronary Thrombosis.**—Early writers on coronary thrombosis directed attention to the fact that the disease might closely simulate surgical conditions in the upper abdomen, and the possibility of erroneously attributing the symptoms of coronary occlusion to upper abdominal disease has since been emphasized repeatedly. The pain of coronary thrombosis may

be situated *entirely in the upper abdomen* for several hours, and on examination there may be muscle spasm and tenderness in the epigastrium or right upper quadrant. These findings and the occurrence of fever, leukocytosis, vomiting and at times jaundice may very strongly suggest *biliary colic, perforated peptic ulcer, acute intestinal obstruction, or acute pancreatitis*.

An error in diagnosis usually can be avoided, however, by careful attention to the *clinical history* and to other points in the general physical examination. A large proportion of patients who have coronary thrombosis have had *earlier attacks* of typical angina pectoris, and in others there will be a history of "*indigestion*" on effort. The pain of coronary occlusion usually is accompanied by *dyspnea*, while dyspnea is not commonly present in patients who have acute surgical conditions in the abdomen. Furthermore, although the pain of coronary thrombosis may be confined to the epigastrium for several hours, it is much more common to have at least some spread to the *retrosternal area* within a short time of its onset. Radiation of this kind does not occur in abdominal disease.

Physical examination soon after the onset of coronary thrombosis frequently reveals *great weakness of the heart tones*, and *gallop rhythm* is often present. *Pulsus alternans* may be detected while recording the blood pressure, and in patients with extensive cardiac infarction, *râles* may appear over the base of the lungs within a very short time. A *pericardial friction rub* is detected in 10 or 15 per cent of all patients with myocardial infarction and usually develops within one to three days after the onset of symptoms. Its occurrence in patients who have experienced symptoms that might be due to coronary thrombosis furnishes a valuable diagnostic sign. Finally, the *electrocardiogram* may show pathognomonic evidence of coronary occlusion within a few hours of the onset of symptoms.

A few words of caution might well be introduced at this place. In the past, in discussions of the *differential diagnosis* of angina pectoris and coronary occlusion, emphasis has been placed almost entirely upon the fact that these conditions

may closely simulate upper abdominal disease. Of late, however, a few observers have pointed out the possibility that errors may be made in the reverse direction and have reported cases in which symptoms due to gallbladder disease, perforated peptic ulcer, or diaphragmatic hernia suggested coronary artery disease. In the great majority of cases, the presence of angina pectoris or coronary thrombosis is correctly recognized, but as the result of the popularity of these diagnoses, other diseases with similar symptoms undoubtedly are being included at times under the same classifications. Although such errors are not common, they are of importance because of their bearing on prognosis and treatment.

*Other Cardiovascular Conditions.*—There are a few other cardiovascular conditions which may cause severe abdominal pain. Chief among these are aneurysm of the abdominal aorta and infarction of the kidneys, spleen, or mesentery due to emboli from the heart.

*Aneurysm of the abdominal aorta* is of rare occurrence, but it may cause pain, usually constant and boring in character and often very severe, due to pressure upon the spine and nerve roots.

The two most common cardiac conditions which may be complicated by *embolic infarction* of abdominal structures are *bacterial endocarditis*, with the development of large friable vegetations upon the heart valves and endocardium, and *coronary occlusion*, with infarction of the heart and the secondary formation of a mural thrombus over the endocardial surface of the myocardial infarct. Occasionally also, embolic accidents occur in patients with *mitral stenosis* and *auricular fibrillation*. In these patients the auricular appendages often contain thrombotic material, portions of which may be broken off and lodge in any part of the pulmonary or systemic circulation.

*Infarction of the spleen, kidneys, or mesentery complicating bacterial endocarditis* seldom causes confusion in diagnosis. The history of a febrile illness of variable duration, the occurrence of petechiae in the skin or conjunctivae, and the presence

of cardiac murmurs generally lead to prompt recognition of the primary condition, and the obtaining of a positive blood culture establishes the diagnosis beyond doubt. Embolic accidents which complicate coronary occlusion occur most commonly during the second week after the attack but may occur up to the sixth or eighth week. Under unusual circumstances it may happen that the symptoms of coronary occlusion are of such mildness that their significance is not appreciated by the patient or the physician. The development of severe abdominal pain at some time during the following few weeks may then present a difficult problem and may lead to an erroneous diagnosis of acute intestinal obstruction, acute pancreatitis, or perforated peptic ulcer. A careful review of the clinical history, however, should enable one to avoid such a mistake. Embolic accidents which occur in patients with mitral stenosis and auricular fibrillation seldom offer difficulty in diagnosis if the possibility of this complication is kept in mind.

**Summary.**—Dysphagia, anorexia, nausea, vomiting, jaundice, and abdominal pain are not infrequently due to cardiovascular disease. Dysphagia due to compression of the esophagus may result from aneurysm of the aorta, marked enlargement of the left auricle in mitral valve disease, or extensive pericardial effusion. Anorexia, nausea, and vomiting are common manifestations of congestive myocardial failure and are due to congestion of the liver and the mucosa of the stomach and intestinal tract. Nausea and vomiting may also constitute a prominent symptom of coronary artery disease, and especially acute coronary artery occlusion. Jaundice in patients with heart disease is the result of anoxemia of the liver cells and may occur in congestive heart failure, coronary thrombosis, and occasionally in subacute bacterial endocarditis.

Abdominal pain due to congestion of the liver is present in many patients with congestive heart failure, while in angina pectoris and coronary occlusion, the pain may be confined entirely to the upper abdomen. Severe abdominal pain may also result from an aneurysm of the abdominal aorta and from infarction of the spleen, kidneys, or mesentery due to emboli

which arise from the vegetations of bacterial endocarditis, a mural thrombus secondary to myocardial infarction, or from thrombi in the left auricular appendage in patients with mitral stenosis and auricular fibrillation.

While, at times, any of these symptoms may sufficiently dominate the clinical picture to suggest primary gastro-intestinal disease, attention to the details of the clinical history and a thorough physical examination usually enable one to make the correct diagnosis.





**Review of the Literature.**—In 1925, Boas and Shapiro<sup>2</sup> described five cases of hypertension in which the basal metabolic rates were elevated. Four of these five patients were women, and four of the five had persistent tachycardia with pulse rates from 110 to 140. The authors concluded that these cases constitute a special syndrome which should be distinguished from the ordinary form of hypertension as well as from exophthalmic goiter.

Rose<sup>3</sup> reported the case of a woman who had malignant hypertension associated with tachycardia and an elevation of the basal metabolic rate. This patient obtained no clinical relief following subtotal thyroidectomy, and the basal metabolic rate remained elevated after the operation.

Liljestrand and Stenström,<sup>4</sup> Boothby and Sandiford,<sup>5</sup> Keith, Wagener and Kernohan,<sup>6</sup> Händel,<sup>7</sup> Mannaberg,<sup>8</sup> and Brocker and Kempmann<sup>9</sup> have also studied the elevation of the basal metabolic rate which sometimes is associated with hypertension, and Hamilton and Beck<sup>10</sup> have presented cases of hypertension in which the presence of high basal metabolic rates rendered difficult the differentiation from hyperthyroidism. Although it has been suggested that increased cardiac work or overactivity of the endocrine glands may be responsible for the increased metabolism in these cases, no completely satisfactory explanation of the syndrome has been made.

**Presentation of Material.**—During the past five years, eighteen cases (table, p. 397) of severe essential hypertension associated with hypermetabolism have been studied with reference to thyroid activity. Although appropriate studies ruled out the presence of hyperthyroidism in every case, four of these eighteen patients had been told elsewhere that hyperthyroidism was present and that subtotal thyroidectomy was indicated. In three additional instances, hyperthyroidism was suspected at the time of the first examination in the clinic. This suggests the frequency with which severe essential hypertension is confused with hyperthyroidism, an error which can easily be made when the extent of the changes associated with severe hypertension is not appreciated.

Age	Systolic pressure	Diastolic blood pressure	Papillation	Pulse rate	Loss of weight in pounds	Nervousness	Heart-disease	Tremor	Exophthalmos	Goiter	Before entry	At clinic. Question of hyperthyroidism.	Basal metabolic rate.	Iodine, micrograms per 100 cc.	Thyroid soluble per 100 cc.	Hyperthyroidism (mild)	Hyperthyroidism (benign)
40	100	130	0	90	35	0	0	0	0	0	✓	0	+17	..	..	✓	
35	220	160	✓	90	28	✓	0	0	0	0	0	0	+23	..	..	✓	✓
41	280	170	✓	90	12	✓	✓	0	0	0	0	0	+30	8.4	204	✓	
63	190	120	0	74	15	✓	✓	0	0	0	0	0	+18	..	..	✓	✓
37	220	160	✓	100	65	0	✓	✓	0	0	0	✓	+77	8.1	191	..	✓
39	190	140	✓	140	5	✓	✓	0	0	0	0	0	+41	28.0	140	✓	
55	210	120	✓	131	40	✓	0	0	0	✓	✓	✓	+30	9.1	400	..	✓
42	210	140	0	110	25	0	✓	✓	0	0	0	0	+15	..	..	✓	
41	260	160	✓	101	27	✓	0	✓	0	0	0	✓	+23	11.3	210	✓	✓
32	280	170	✓	120	16	✓	✓	0	0	0	0	0	+44	..	120	✓	
62	220	133	✓	108	30	0	✓	✓	20 min. apparent	✓	✓	✓	+59	7.0	..	✓	
48	270	160	✓	122	47	0	✓	0	0	✓	0	✓	+47	..	..	✓	
31	250	160	✓	108	68	0	✓	0	0	0	0	0	+25	21.8	187	✓	
48	220	160	0	96	no stat.	0	✓	0	0	0	0	0	+15	23.2	213	✓	
62	200	160	0	101	16	✓	✓	✓	0	0	0	0				✓	
57	220	140	✓	90	40	0	0	Coarse	0	0	0	0	+21	18.6	204	✓	
27	220	120	✓	100	10	0	0	✓	0	St. diffuse	0	0	+43	16.6	..	✓	✓
42	260	140	✓	85	no stat.	✓	✓	0	apparent, not real	0	Ind. thyroidectomy without relief	0	+41	16.8	136	..	✓
Average 43	232	145	72%	101	28.5	50%	61%	41%	11.1% apparent, not real	10.6%	22.2%	27.7%	+33%	15.3	203.5	77.7%	22.2%

*Symptoms* suggestive of hyperthyroidism are commonly associated with severe hypertension. *Palpitation* was a leading symptom in 72 per cent of the cases. The average pulse rate of the eighteen patients in this group was 104, and in 61 per cent the pulse rate was over 100. Fifty per cent of the patients complained of *nervousness*. A *loss of weight* was a nearly constant finding, the average loss being 28.5 pounds. A *tremor*, usually coarse, was present in 44 per cent of the cases. The thyroid gland was palpably *enlarged* in 16.6 per cent of the cases, and although measurable exophthalmos was present in no case, there were two instances in which there was an apparent exophthalmos.

The *blood iodine level* was determined by the method of McCullagh<sup>11</sup> in eleven instances and it was normal or low in five cases, slightly elevated in three cases, and definitely high in three cases. Curtis<sup>12</sup> has shown that hypertension is not infrequently accompanied by inexplicable elevations in the blood iodine level. That there is no correlation between the elevation of the metabolism and the elevation of the blood iodine level is shown by the fact that the blood iodine was elevated in six of the ten cases of hypertension in which there was no associated elevation of the basal metabolic rate. In other words, the blood iodine level may be elevated in cases of uncomplicated hypertension and is hence an unreliable guide to overactivity of the thyroid gland in this condition. A *low* blood iodine level is nevertheless of negative value in ruling out hyperthyroidism.

Hurxthal<sup>13</sup> has demonstrated the significance of a *low blood cholesterol* as an indication of hyperthyroidism. The blood cholesterol was determined in ten cases and in seven of the ten cases it was normal or high. In three, relatively low cholesterol figures were obtained (120, 136, and 140, respectively). In one of the cases in which low cholesterol values were obtained, thyroidectomy had been performed recently without relief of symptoms, and in the other two instances there was no palpable enlargement of the thyroid gland.

Peabody<sup>14</sup> has shown that the *basal metabolic rate* is often

elevated in the presence of severe cardiac decompensation and that this elevation usually occurs only when the patient is dyspneic at rest. The high basal metabolic rates in this series could not be attributed to cardiac failure because evidence of cardiac decompensation was present in only three of the cases and in no instance was the decompensation severe enough to cause dyspnea at rest. The difficulty of evaluating the role of the thyroid gland in the production of these changes cannot fail to be apparent, especially in those cases in which a goiter was present coincidentally.

**Illustrative Cases.**—The following cases of severe hypertension illustrate the not uncommon findings in this condition of a *persistent tachycardia*, a *history suggestive of hyperthyroidism*, and an *elevation of the basal metabolic rate*:

*Case I.*—The patient was a married woman, forty-eight years of age, whose chief complaints were loss of 47 pounds in weight, weakness, and loss of vision in the left eye. Three years before admission the patient had been told that she had a goiter, but she had never noticed any change in the size of her neck. She had noted no nervousness or hyperhidrosis, and her appetite was poor. She had been referred to the Clinic for the purpose of determining whether or not hyperthyroidism was present.

Examination showed pallor and undernutrition. The patient's behavior was quiet and expressed fatigue rather than stimulation. The skin was warm and slightly moist. A very slight, irregular tremor of the outstretched hand was present. The eyes were described as prominent and measured 20 mm. in the anteroposterior position, a figure which is within the limits of normal. The palpebral fissures were within normal limits but were unequal, the right measuring 11 mm. and the left 8 mm. Examination of the fundi showed high chocking of the discs and marked retinal changes consistent with the presence of malignant hypertension. There was a firm, nodular enlargement of the thyroid gland to about twice its normal size. The lungs were clear except for a few râles at

the right base. The heart was enlarged to the left, and a systolic murmur was audible at the apex and in the aortic area. There was no dyspnea or edema, and the liver could not be palpated. The pulse rate was 122 and the blood pressure was 265 mm. systolic and 160 mm. of mercury diastolic. The rest of the physical examination showed no abnormal findings.

The patient entered the hospital where, in spite of a normal temperature, her pulse at rest in bed varied between 100 and 120 for the first two days. The systolic blood pressure was consistently found to be around 240 mm. and the diastolic around 140 mm. of mercury. There was a secondary anemia, with 4,090,000 red blood cells, and 61 per cent hemoglobin. The Wassermann and Kahn tests gave negative reactions. Examination of the urine showed a few granular and hyaline casts. The urea clearance was 38 per cent in the first hour and 33 per cent in the second, and the blood urea was 60 mg. per 100 cc. A roentgenogram of the chest showed an enlarged heart and pulmonary fibrosis.

Duplicate basal metabolic rates on two separate occasions averaged plus 56 per cent and plus 47 per cent, respectively, but the blood iodine value was only 7 micrograms per 100 cc., a figure which is at the lower level of normal.

In view of the low blood iodine level and because the behavior of the patient was not typical of hyperthyroidism, a diagnosis of nodular goiter without hyperthyroidism, and malignant hypertension was made.

On the sixth day after the patient's admission to the hospital, she suddenly became unconscious and died soon after. Permission for autopsy was not granted.

*Case II.*—The patient was a married woman, forty-two years of age, whose chief complaints were weakness, substernal pain, smothering and choking sensations, loss of 25 pounds in weight, nervousness, and sleeplessness. These symptoms had been present for the preceding eight months, and she had been told that she had high blood pressure and "clinical signs and symptoms of goiter." The patient had been referred to the

Clinic to determine whether or not hyperthyroidism was present.

Examination showed an apparent prominence of the eyes without any widening of the palpebral fissures or lid lag. Measurements, however, showed that no true exophthalmos was present. There was a small diffuse goiter over which no thrill or bruit could be detected. The heart was enlarged; the lungs were clear. The liver could not be palpated, no edema was present, and there was no dyspnea at rest. A presystolic gallop rhythm and a systolic apical murmur were heard. The systolic blood pressure was 210 mm. and the diastolic 140 mm. of mercury; the pulse rate was 116. The pulse rate remained consistently above 110 during the two weeks' period in the hospital. Duplicate determinations of the basal metabolic rate while the patient was at rest in bed averaged plus 30 per cent. The blood cholesterol, however, was 400 mg. per 100 cc. and the blood iodine was 9.1 micrograms per 100 cc.

Laboratory studies showed a trace of albumin as well as red blood cells and casts in the urine. There was a slight secondary anemia with 4,900,000 red cells and 71 per cent hemoglobin. The blood urea varied from 36 to 45 mg. per 100 cc. The Wassermann and Kahn tests gave negative reactions. The urea clearance was 62 per cent at the end of the first hour and 49 per cent at the end of the second hour. Electrocardiograms showed left bundle branch block. All other laboratory studies gave findings within normal limits.

Despite the tachycardia and the elevation of the basal metabolic rate, the finding of a low blood iodine and a high cholesterol level, as well as the absence of the typical clinical features of hyperthyroidism, enabled us to rule out the presence of hyperthyroidism. A diagnosis of malignant hypertension was made and a poor prognosis was given.

*Case III.*—This patient was a married woman, thirty-two years of age, who complained of severe headaches which had been present for ten years and of palpitation and dyspnea on

exertion in the past three months. She had lost 15 pounds in weight.

Physical examination showed that the thyroid gland was not enlarged. The heart was enlarged to the left but the lungs were clear. There was no edema, the liver was not enlarged, and there was no dyspnea. The blood pressure was 260 mm. systolic and 160 mm. of mercury diastolic when the patient was at rest in bed. The pulse rate was consistently found to be between 110 and 130. Examination of the fundi showed bilateral choking of the optic discs. Electrocardiograms showed myocardial damage, and the urine showed a trace of albumin. A secondary anemia was present, with 4,640,000 red cells and 61 per cent hemoglobin. The blood urea was 30 mg. per 100 cc. The Wassermann reactions were negative. Duplicate determinations of the basal metabolic rate averaged plus 23 per cent, but the blood cholesterol level was 210 mg. per 100 cc. and the blood iodine average 11.3 micrograms per 100 cc., a figure within normal limits.

Despite the tachycardia and elevation of the basal metabolic rate, the finding of normal blood cholesterol and iodine values, as well as the clinical appearance of the patient, ruled out the presence of hyperthyroidism and a diagnosis of malignant hypertension was made.

*Case IV.*—The patient was a married woman, forty-two years of age, who complained of high blood pressure, headaches, dizziness, blurring of the vision, palpitation, dyspnea on exertion, and fatigue. She had known that for seven years she had high blood pressure. Two years before entry a subtotal thyroidectomy had been performed by an excellent surgeon in another city, but the patient had obtained no symptomatic relief except for some decrease in the choking sensations that had troubled her before the operation.

The pulse rate on admission was 90 and the blood pressure was 270 mm. systolic and 120 mm. of mercury diastolic. There was no tremor and the hands were warm and dry. No thyroid tissue was palpable. There was no exophthalmos or widening

of the palpebral fissures. The heart was enlarged to percussion and there were both systolic and diastolic murmurs in the aortic area. The lungs were clear, there was no edema, and no enlargement or tenderness of the liver. There was no history of rheumatic fever. The fundi showed haziness of the discs and extensive changes in the vessels consistent with an early malignant hypertension.

A roentgenogram of the chest showed a large heart and a moderate degree of chronic passive pulmonary congestion. Examination of the blood showed 4,490,000 red cells, 10,350 white cells, and 65 per cent hemoglobin. The blood volume was 88 cc. per kilogram of body weight. An electrocardiogram showed left axis deviation and a diphasic T wave in lead III. The Wassermann and Kahn reactions were negative, and the urea clearance test showed 41 per cent clearance in the first hour and 56 per cent clearance in the second hour, with a blood urea of 36 mg. per 100 cc.

The cold pressor test was strongly positive, the diastolic blood pressure rising from 130 to 165 mm. of mercury and the systolic from 165 to a level too high for a reading to be obtained on the manometer one-half minute after the patient immersed her hand in ice cold water.

The blood velocity as measured by intravenous injection of sodium decholate was 32 seconds and 26 seconds on two separate trials. Although the patient was not pregnant, the Friedman test was strongly positive, showing 4+ hemorrhagic follicles. The blood iodine was 16.8 micrograms per 100 cc. and the blood cholesterol was 136 mg. per 100 cc. Duplicate determinations of the basal metabolic rate on two separate occasions were plus 41 per cent and plus 31 per cent, respectively.

In spite of the high basal metabolic rate, the high blood iodine and the low blood cholesterol levels, hyperthyroidism could be ruled out definitely, not only by the absence of its clinical signs, but from the fact that the patient did not improve following the subtotal thyroidectomy that had been performed elsewhere. The final diagnoses were therefore:

malignant hypertension, hypertensive heart disease and aortic insufficiency.

**Discussion.**—In these four illustrative cases, the *tachycardia* and the *elevation of the basal metabolic rate* could not be explained on the basis of cardiac decompensation; nor did it seem likely, in view of the *high cholesterol* and *low blood iodine values* obtained in three cases and absence of improvement after thyroidectomy in the fourth case, that the elevation of the basal metabolic rate was the result of *hyperthyroidism*. In all four cases, therefore, the hypermetabolism was in all probability intimately connected with or the result of the severe hypertension.

In *excluding hyperthyroidism* in patients with severe hypertension, the fundamental principle of diagnosis must be followed, and this is the undesirability of making two diagnoses when the entire clinical picture can be explained on the basis of a single disease. Since malignant hypertension and hyperthyroidism probably bear no etiologic relationship to each other, their co-existence is necessarily uncommon. The diagnosis of hyperthyroidism should, therefore, be made *with caution* in patients presenting the characteristic features of severe hypertension.

Despite the similarity of the symptoms and physical findings observed in these two conditions, the behavior of the patient with malignant hypertension is likely to be *less stimulated* and *hyperkinetic*, and the movements are apt to lack the quickness that is so characteristic of every activity of the patient with typical hyperthyroidism. Although the *eyes* in cases of malignant hypertension may be prominent even to the point of measurable exophthalmos, there is not as much widening of the palpebral fissures as is seen in association with a corresponding degree of exophthalmos in cases of hyperthyroidism. The staring expression is lacking and the lid lag is usually absent. The *tremor* of the outstretched hand tends to be coarser and more irregular than that seen in hyperthyroidism. Although the *appetite* is often good, it is not apt to be so strikingly increased as is the case in patients with hyperthyroidism.

And lastly, if *loss of weight* is present, it is often attributable to special diets which the patients have been following. In spite of these differences in the clinical picture, the examiner may be misled by the persistence of the tachycardia and by the finding of consistently high basal metabolic rates. In such cases the *determination of the blood iodine and cholesterol levels* are of definite value.

**The Etiology of the High Basal Metabolic Rate in Hypertension.**—The most obvious interpretation of the increased metabolism in patients with malignant hypertension is that there is an associated overactivity of the thyroid gland. It is unlikely, however, that this is the case, because the blood iodine and cholesterol levels are usually within normal limits and the clinical features of true hyperthyroidism are absent.

One of us has recently studied an interesting case on the service of Dr. Glover Copher of St. Louis. This case further supports the hypothesis that some factor *other than the thyroid gland* is responsible for the elevation of the basal metabolic rate in patients with malignant hypertension. The patient was a woman, thirty-nine years of age, who was suffering from malignant hypertension. She complained chiefly of orthopnea and paroxysms of dyspnea. The blood pressure was 220 mm. systolic and 160 mm. of mercury diastolic, and there was bilateral choking of the discs and retinal changes consistent with malignant hypertension. Repeated basal metabolic rates averaged plus 46 per cent when the patient was at rest in bed in the hospital. The pulse rate, however, was normal. No enlargement of the thyroid gland could be palpated, there had been no loss of weight and no increase of appetite, and the basal metabolic rate was not reduced by a course of iodine therapy, nor was there any improvement in the symptoms during this treatment.

A total ablation of the thyroid gland was performed by Dr. Copher on June 8, 1934 in the hope of restoring cardiac compensation. This procedure was followed by complete relief from the attacks of dyspnea and palpitation, but the blood pressure was not appreciably affected. Four months after the

thyroidectomy, the basal metabolic rate was still plus 7 per cent. The patient died with a ruptured aorta one month after this test and postmortem examination showed no trace of thyroid tissue. Small bilateral cortical adenomata of the adrenal glands and bilateral follicular ovarian cysts were found. Unfortunately, permission to remove the pituitary gland was not obtained.

This case is of special interest because it demonstrates conclusively that in the proved absence of all thyroid tissue, it is possible for a patient with hypertension to maintain a basal metabolic rate of plus 7 per cent. The basal metabolic rate fell only 39 points following total ablation of the thyroid gland and it remained within normal limits instead of falling to the usual myxedematous level of from minus 30 to minus 40 per cent. This indicates that the increased metabolism in this case was the result of some factor other than thyroid overactivity.

If the increased metabolism associated with hypertension is not secondary to thyroid hyperactivity, an alternative explanation is that it might be the result of an overactivity of other glands of internal secretion, notably the *pituitary* and *adrenals*. In support of this theory, there is the occasional finding of endocrine dyscrasias in patients with hypertension, such as the small adrenal cortical adenomata that were found in Copher's case. Chromaffin-cell tumors of the adrenal gland have been found in patients with severe (usually paroxysmal) hypertension,<sup>15</sup> and pituitary adenomata have also been reported associated with hypertension, as for example, in Cushing's syndrome of pituitary basophilism<sup>16</sup> and in acromegaly. Lastly, we have observed in several cases of severe, essential hypertension, a measurable increase of the gonadotropic pituitary hormone as indicated by a strongly positive *Friedman* test.

Although it is possible that the increase of the basal metabolic rate in certain cases of severe essential hypertension could be the direct result of the overactivity of one or more of these glands of internal secretion, the endocrine findings in hypertension are so rarely abnormal that it is possible the

increase of metabolism found in many cases of severe hypertension is *completely unrelated to the activities of the glands of internal secretion*. This view is substantiated by the fact that an increase of metabolism is not a constant finding in the pituitary basophil syndrome, in the presence of an excess of prolactin, or in patients with adrenal cortical or chromaffin-cell adenomata. There is, however, good experimental evidence which shows that certain pituitary extracts are capable of causing striking elevations in metabolic rates in thyroidectomized animals<sup>17</sup> and in men.<sup>18</sup>

The other possible explanation for the increase of the basal metabolic rate in hypertension is that it is a purely *mechanical* reaction, involving an increase in the work of the heart in maintaining circulation against high diastolic pressure. This results in an increase of oxygen consumption by the myocardium, hence in an increase of the oxygen consumption of the body at rest and in a proportional increase of the basal metabolic rate. In addition, the hypertension may cause an increase in the work and in the oxygen consumption of the smooth muscles of the arteries and arterioles throughout the body, thus further increasing the oxygen consumption and the basal metabolic rate.

In testing this hypothesis, we have observed elevations of the basal metabolic rate of from plus 21 to plus 56 per cent in a number of conditions in which excessive work is imposed upon the myocardium.

In two patients who had huge vascular pulsating tumors over which a loud bruit could be heard and a distinct thrill felt, one of which was a metastasis from a malignant adenoma of the thyroid and the other a hypernephroma, all the features of an arteriovenous fistula were present. The heart was enlarged, the pulse pressure increased, and there was a persistent tachycardia. Despite the finding of basal metabolic rates of plus 56 per cent and plus 26 per cent, respectively, no clinical evidence of hyperthyroidism was present, and the blood iodine and cholesterol levels were normal. Likewise, in an uncomplicated case of posttraumatic arteriovenous fistula,

there was a persistent tachycardia, cardiac enlargement, and a basal metabolic rate of over plus 20 per cent on two occasions.

These cases are included merely to emphasize the rôle that increased work and increased oxygen consumption of the myocardium may play in the production of changes in the basal metabolic rate. It is still not clear, however, why hypermetabolism is present in one case of hypertension and absent in the next although the blood pressure may be equally high in both cases. Neither have we been able to explain why the high metabolic rates were more common in women, nor why they usually were associated with tachycardia and not so often observed in cases in which the pulse rate is normal.

**Summary.**—1. Uncomplicated severe hypertension can produce a syndrome characterized by a persistent tachycardia and an elevation of the basal metabolic rate accompanied by symptoms and signs suggestive of hyperthyroidism.

2. A case of hypermetabolism independent of thyroid overactivity and associated with severe hypertension is reported. The basal metabolic rate was plus 7 per cent four months after a proved total ablation of the thyroid gland.

3. The importance of ruling out hyperthyroidism and avoiding a futile subtotal thyroidectomy in certain cases of severe essential hypertension is emphasized.

4. Certain clinical and laboratory criteria, especially the appearance and behavior of the patient and the determination of the blood iodine and blood cholesterol levels, are of value in ruling out hyperthyroidism.

5. The cause of the elevation of the basal metabolic rate in patients with hypertension is discussed, and it is suggested that this elevation may in part be the result of the increased cardiovascular activity involved in maintaining the circulation against the high diastolic blood pressure. The possibility of pituitary hyperactivity as a factor should be considered.

(We wish to express our thanks to Dr. Glover Copher for permission to report his case.)

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## ROENTGENOLOGIC DIAGNOSIS OF RENAL TUMORS' WITH AN EVALUATION OF EXCRETORY UROGRAPHY

B. H. NICHOLS

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THE diagnosis of renal neoplasms is probably one of the outstanding developments of medical diagnosis. Hinman furnishes us the following quotations:

From Kelly in 1898: "A report was made that 70 per cent of all malignant tumors of the kidney in his service came to necropsy without a diagnosis and only two cases in the series were without metastases to the lungs or liver." From Kroenlein in 1905: "The signs and symptoms of malignancy of the kidney are so insufficient that only one case in twenty may be correctly diagnosed." From Hyman in 1928: "The average five-year cure of cancer of the kidney by surgery does not exceed 15 per cent."

When one considers the high rate of mortality associated with renal tumors and the advanced stage of the disease, even to metastasis, he is at once impressed with the importance of any new developments in diagnosis. The difficulty of such an accomplishment is evident when we realize that less than 50 per cent of malignant renal neoplasms have no demonstrable urinary symptoms and are accompanied by a *normal* urinary report, which is too often considered sufficient to exclude disease of the kidney. The presence of normal urine should receive little consideration for or against tumor; there are many other causes for hematuria and there are many kidney tumors without hematuria. Perhaps the fact that we are not sufficiently "kidney conscious" adds much to the failure of early diagnosis in many cases.

Pyelography is a most valuable method for the investigation of lesions in the kidney. However, the more recent de-

velopment of excretory urography is an added diagnostic procedure which may be applied to almost any individual, from the extremes of old age to childhood. This method offers little excuse for not investigating the kidney on the least suspicion. Excretory urography can be done quite satisfactorily wherever roentgen service is available and we believe that at the present time it is available in all hospitals of the United States.

The most important item, then, is constantly to reiterate the *possibility of kidney lesions in the presence of hematuria, pain in the upper abdomen or back, and a palpable mass in the region of the kidney*. None, or any number of these symptoms, however, may be present.

**Pain.**—The patient presenting *pain in the back* should first have a roentgen examination of the spine in an attempt to eliminate bone or joint disease in the spine which might account for the symptoms. This examination should visualize the size, shape, and position of the kidneys. If there is a definite irregularity of either kidney with enlargement of either the upper or lower pole or of the entire kidney itself, *excretory urography* should be performed or a *pyelogram* made of the suspected kidney in order to determine the presence or absence of a tumor. Too frequently after the clinical history is obtained the patient is submitted to examination of the gastro-intestinal tract, including the gallbladder and the colon. These examinations may all prove negative for pathologic change, and the presence of barium in the intestinal tract handicaps further examination of the urinary tract so that the latter should be done whenever possible before the gastro-intestinal examination is undertaken. However, if examination of the spine and gastro-intestinal tract reveals no evidence of pathologic change which could account for the pain, the urinary tract should be studied carefully.

It is evident, then, that the records should show examinations of many normal kidneys in order that a rather small percentage of tumors may be observed at an early date and at a time when treatment is most successful. If a filling defect

which simulates a tumor is found, by the law of probability it is *malignant*, as most of the tumors of the kidney are of this character. It is only by such thorough examination that we can hope to diagnose early tumors of the kidney and thereby reduce the number of deaths from cancer. This places an added responsibility, however, on roentgenologists, because, the smaller the lesion, the greater the difficulty in diagnosis.

*In the presence of a tumor*, the interpretation of the *intravenous pyelogram* is usually more difficult than that of the *retrograde pyelogram*. In excretory pyelography the kidneys are not well filled and many times it is quite easy to misinterpret a filling defect which might be definitely diagnosed by retrograde pyelography. This should usually follow the intravenous examination if there is any question about the identity of the lesion. On the other hand, because of the fact that the kidney is poorly filled and there are no classical symptoms of tumor, we should not attempt to exclude tumor, which would only add to the presence of a more advanced, possibly inoperable, lesion. This applies particularly to tumors of the renal pelvis. Cortical tumors will often produce sufficient deformity in the excretory urogram definitely to diagnose a tumor. The determination that a tumor is malignant or benign may offer some difficulty. However, if the vast majority of tumors are malignant, it is best to err on the safe side by at least making a tentative diagnosis of malignancy and insisting on further examination at rather short intervals until one is certain the lesion is not undergoing further development.

Malignant tumors of the kidney, excluding encapsulated hypernephroma, *invade the kidney structure very early*. If we can determine this, we can be quite sure that the lesion is probably a malignant tumor; that is, if infection can be excluded.

**Hematuria.**—If hematuria is present, we are frequently confronted with the presence of *blood clots* in the kidney. These are of aid in calling attention to the possibility of a tumor, but they often make diagnosis quite difficult on account of the *filling defects* found in the pyelogram which may closely

simulate a papilloma of the kidney or a stone. The *repetition* of a urogram at intervals of a few days usually will exclude such a difficulty, as either the filling defect will be changed or the clots will be absent.

**Palpable Mass.**—In the presence of a palpable mass, excretory urography usually will be adequate and may either show the mass outside the kidney by a normal pyelogram of the kidney on the side of the mass, or show a definite filling defect if the kidney is functioning, demonstrating the presence of a tumor of the kidney.

Perhaps we might consider briefly a few of the more important tumors:

**Hypernephroma.**—Hypernephroma is the most common type of renal tumor. This term is quite convenient from a clinical standpoint as the growth is usually encapsulated and, as it does not invade kidney tissue early, at least, it seems a distinct clinical entity. Many pathologists, however, feel that hypernephroma is simply a type of carcinoma, which is probably true. However, I think that most physicians are quite familiar with its characteristics. Hypernephroma constitutes about 65 to 85 per cent of all the malignant lesions of the kidney. These tumors usually metastasize late and, as previously stated, show little tendency to infiltrate the kidney or surrounding structure. A small number, however, infiltrate the venous system early and produce metastases. This is, however, rather an exception. Hypernephroma also shows little tendency to involve the regional lymph nodes and is much unlike a carcinoma. These tumors are found usually in patients between the ages of forty and sixty years. About 75 per cent are found in the lower poles of the kidney. A history of trauma may be of some aid in diagnosis as there are a few cases reported with a definite initial history of trauma. There is no primary precancerous state in hypernephroma which has been satisfactorily demonstrated.

Infection and other lesions of the kidney appear not to contribute to the etiology of hypernephroma. The *clinical symptoms* are *hematuria*, *pain*, and a *palpable tumor*. One,

all, or none of the above symptoms, however, may be present. It is the consensus of opinion among urologists and authors that hematuria may be found in only 50 per cent of the cases. In our series, the frequency was 53.2 per cent. When it is present, it is valuable in directing attention to the kidneys. The bleeding is intermittent, of rather short duration; it may be the only symptom and remain so for a long time. A tumor mass may not appear until after many attacks of hematuria, but in our series a sizable tumor appeared usually within one year after the first attack of hematuria. A palpable mass may be the sole symptom. In our series, 75 per cent of all cases coming to operation had a palpable mass. Pain occurs in about 35 per cent of the cases. In the presence of a hypernephroma, there may also be *fever*. If metastasis occurs early, the presenting symptom may be a *fracture*. Where there is a fracture with a complete osteolytic lesion in the bone, the kidney should be investigated immediately for the possibility of hypernephroma, provided no other recognized primary lesion is present.

**Carcinoma of Renal Pelvis.**—Carcinoma of the pelvis of the kidney offers considerable difficulty in diagnosis. These are early, small, localized lesions of the kidney pelvis and are of the *papillomatous* type (which may be either benign or malignant) or are of the *sessile* type (which includes squamous cell carcinoma or epidermoid carcinoma). These lesions are prone to hematuria, which may render diagnosis difficult on account of the *blood clots* in the kidney pelvis. The smallness of the lesion and the single area of occupation will be confused many times with pelvic renal tuberculosis. We have observed twelve cases of carcinoma of the renal pelvis in our series. There were four patients with squamous cell carcinomas who were dead within six months; three with papillary carcinomas living one year; one with squamous cell carcinoma living nine months; two with papillary carcinomas well for four years; and two with papillary carcinomas living and well two months.

*Excretory urography* is usually rather *inadequate* for the

diagnosis of these lesions, owing to the rather restricted filling of the kidney pelvis. In all of our cases it was therefore necessary to make a *retrograde pyelogram*.

*Adenocarcinomas* reveal a rather large, well-outlined filling defect and in many cases may be diagnosed by excretory urography. It is still better, however, to confirm the diagnosis by an additional pyelogram.

**Comment and Summary.**—It is evident, then, that urography contributes much to the diagnosis of renal tumors. It must not be forgotten, however, that the urologist may gain much valuable information by *cystoscopy* and *catheterization* of the ureters. The hematuria may be coming from the bladder, and it can also be determined whether the blood is coming from the right or left kidney. Retention, function, or the presence of a papilloma in the bladder can by this means be determined.

The proper procedure for the diagnosis of renal neoplasms is therefore a comprehensive, thorough correlation of all the radiologic findings, the clinical symptoms, and the urologic findings. It is only by such means that we can hope to reduce the mortality from cancer of the kidney. The following is a group of tumors representing the radiologic findings:

#### ILLUSTRATIVE CASES

Figure 42: Shows a large, smooth, regular tumor mass at the lower pole of the right kidney producing obstruction of the ureter and hypernephrosis. The lesion was a large, benign solitary cyst of the kidney.

Figure 43: Man, fifty-four years old. Painless hematuria for two months. Some frequency, nocturia and pain in the lumbar region. The pyelogram shows a filling defect in the kidney pelvis produced by a papillary carcinoma.

Figure 44: Man, fifty-seven years of age. Pain in the left side and hematuria for the past six months. Cystoscopy shows a papilloma of the bladder. The pyelogram shows a tumor of the kidney, a large papilloma in the upper pole, with transplant to the bladder.



Fig. 42.



Fig. 43.



Fig. 44.



Fig. 45

Figure 45: Man, forty years of age. Lumbago and pain in the left kidney region. Three years ago he had hematuria and passed three stones. Present symptoms of seven weeks' duration. Pyelogram shows a nonopaque stone in the pelvis of the left kidney. Such deformity may be mistaken for a papilloma of the kidney. However, the history of previous stones suggests the diagnosis of nonopaque renal calculus.

Figure 46: Woman, forty-nine years of age. Hematuria for two years with pain in the left side. Clinical impression:



Fig. 46.

"tuberculosis." Urinalysis negative for tubercle bacilli. The pyelogram shows a defect in the caudal calyx, suspicious for tumor. Operation revealed a squamous cell carcinoma of the kidney.

Figure 47: A, Man, sixty-six years of age. Pain in the left side radiating into the bladder region. Several weeks ago he had an attack of hematuria. He has frequency at present but no blood in the urine. Impression was right renal calculus. The pyelogram revealed irregular multiple filling defects

*A**B*

Fig. 47.

which were believed to be due either to blood clots or tumor. Nephrectomy showed a hypernephroma of the right kidney. Following nephrectomy he had an extensive course of radiation therapy. Three years and three months later a letter from the patient revealed his condition as good, with no evidence of return of tumor. *B*, Specimen of the tumor removed.

Figure 48: Man, fifty-eight years of age. Hematuria and frequent attacks of retention over a period of nine months. Except for hematuria, the urine was normal. Physical findings



Fig. 48.

were negative. Pyelogram shows a large filling defect in the upper portion of the right kidney. Nephrectomy showed a papillary carcinoma. The patient lived five months and three days following operation. Total course of disease, one year, two months and three days.

Figure 49: Woman, forty-three years of age. Complained of kidney trouble for ten years. This trouble consisted of soreness, aching and discomfort on either side of her midabdomen and in the lumbar region of her back. Bilateral pyelo-

grams showed this patient to be suffering from bilateral polycystic kidney. A single pyelogram of either of these kidneys, particularly the left, might easily be mistaken for a tumor.

Figure 50: A man, aged forty-eight years. Attacks of hematuria four years. Previous diagnosis: Polycystic kidney, right side. Urine normal except for blood. Pyelogram shows a large hypernephroma of the right kidney. The pa-



Fig. 49.

tient had an extensive course of x-ray therapy following operation and was alive and well three years after operation.

Figure 51: A man, sixty-seven years of age. Pyelogram was interpreted as a tumor of the left kidney. Nephrectomy revealed a chronic interstitial nephritis. No evidence of tumor. The patient was alive and well four years following operation.

Figure 52: Man, fifty-six years of age. Had two attacks of hematuria, one nine days prior to this examination and one three days. No other urinary symptoms were present. He had no pain. A pyelogram was made on account of previous hema-



Fig. 50.



Fig. 51.

turia, showing a tumor of the upper pole of the left kidney. Nephrectomy was performed and a hypernephroma revealed. The patient lived one year postoperatively.

Figure 53: Man, fifty-seven years of age. Had hematuria, nocturia, intermittent for fourteen months, with pain in right groin. Patient had chronic prostatitis. Pyelogram unable to rule out tumor on account of blood clots in the pelvis and upper ureter. Blood chemistry showed urea, 51 mg. Nephrectomy showed a large nodular irregular kidney with

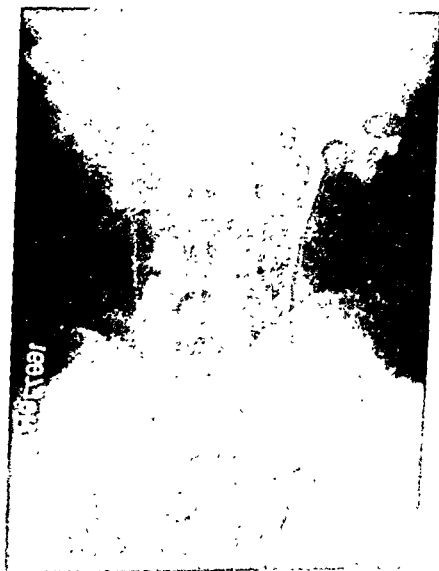


Fig. 52.

a tumor in the upper pole. A hypernephroma. Unable to follow this patient postoperatively.

Figure 54: Woman, fifty-eight years of age. Chief complaint was gastric disturbance, with a severe attack of aching in the stomach relieved by bringing up gas. Physical examination showed a large papillary tumor in the region of the right kidney. The urine was normal except for a slight trace of albumin. Pyelogram shows a large tumor of the right kidney with hypernephrosis. Nephrectomy revealed a large hypernephroma



Fig. 53.



Fig. 54.

of the right kidney. Twelve months after operation the patient died with metastasis to the brain.

Figure 55: Man, forty-one years of age. Intermittent hematuria of one year's duration; no other urinary symptoms. There was a palpable mass in the left upper abdomen about the size of an orange. The pyelogram shows a tumor of the left kidney with a hypernephrosis. Operation revealed a large hypernephroma of the left kidney. This patient has been well for eleven years.

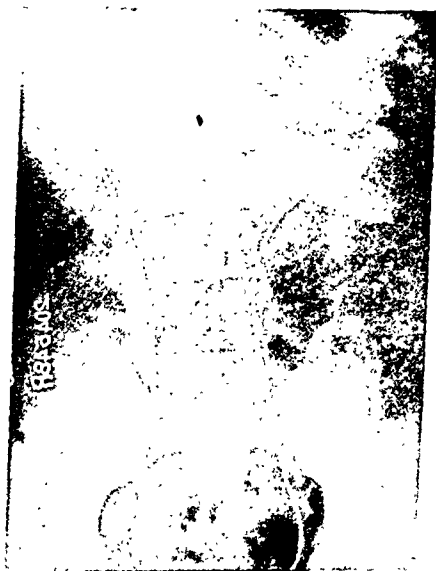


Fig. 55.

Figure 56: Man, seventy years of age. Hematuria three days. No other symptoms. He had had a prostatectomy thirteen years prior to this examination. Plain x-ray film of the abdomen revealed a huge tumor at the lower pole of the right kidney. The pyelogram showed a large tumor of the lower pole of the kidney. The patient had extensive x-ray therapy and right nephrectomy revealed a large hypernephroma of the kidney.

Figure 57: Woman, fifty-one years of age. Chief com-

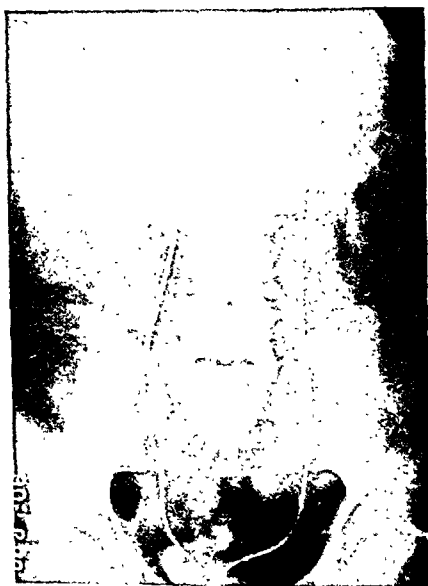


Fig. 56.



Fig. 57.

plaint, stomach trouble and loss of weight of two years' duration. Physical examination revealed a large tumor the size of a grapefruit in the upper left abdomen. The pyelogram shows a large tumor in the upper pole of the left kidney. x-Ray of the chest revealed metastasis. No treatment was instituted. This tumor was found only by a routine examination, and she had no other urinary symptoms. A palpable mass gave the first cue to the presence of the tumor.



Fig. 58.

Figure 58: Woman, fifty-three years of age. Symptoms of frequency with pain in the left flank had been present for two weeks. Palpable mass in the upper left abdomen. The pyelogram shows a large calcified hypernephroma of the left kidney. The diagnosis was confirmed by operation. The patient died two weeks postoperatively from uremia.

## GOUT: A REVIEW OF 62 CASES

JACK KINELL AND RUSSELL L. HADEN

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GOUT is a metabolic disease with varying symptoms and signs. The most common manifestation is *arthritis*, but the joint involvement is usually only a part of the clinical picture. *Chronic nephritis* and *calculi* in the urinary tract, *bursitis*, and *deposits of sodium biurate* in cartilage other than that of the joint surfaces, are common. The disease is evidenced by abnormalities in the *uric acid metabolism*. The exact nature and cause of the metabolic disturbance is unknown. The disease has been variously ascribed to excessive formation of uric acid, to inability of the kidneys to excrete uric acid, and to some derangement of the purine metabolism in which the end products of the purines cannot be disposed of. Talbott and Coombs<sup>1</sup> in a recent study conclude that an increased formation of uric acid rather than diminished excretion or disposal of purines is responsible for the disease.

Gouty arthritis is the most commonly overlooked type of joint disease. Hench<sup>2</sup> thinks that from 5 to 8 per cent of all cases of joint disease studied in an arthritic clinic are gout. Our experience in the Cleveland Clinic bears out this statement. So often gout is undiagnosed because its frequency is not recognized and the joint manifestations are confused with those due to infection or other causes. The acute, swollen, red joint of gout certainly simulates a bacterial infection. We know of one well-known internist who during his own first attack insisted that a surgeon friend incise the involved joint.

Although the fundamental cause of gout is unknown, the common factors precipitating an attack are well recognized: Dietary indiscretions and the excessive use of alcoholic drinks

often are followed by an acute attack if the patient is subject to the disease. The most common type of acute arthritis after surgical operations is gouty arthritis. Attacks seem especially common after operative procedures on the urinary tract where there is usually some diminution of kidney function. Infection may sometimes play a part in the onset of an attack. Heredity is important in the fundamental basis of the disease.

The diagnosis of gout is usually easy if the basic clinical picture is kept in mind; it is often made from the *history* alone. The *typical subject* is an obese, ruddy, otherwise healthy man, engaged in a sedentary occupation. The *onset* is very sudden, and the pain is very severe; usually a single joint is involved at first. The disease often begins in the great toe joint or in the foot, and the pain often begins at night. The affected joint is much *swollen, very red* and *exquisitely tender*. Early in the disease attacks last from a few days to two weeks. There is a gradual *subsidence of symptoms*. Following the acute attack the patient is absolutely free of all joint manifestations. The acute attacks almost always recur after some precipitating influence, as an indiscretion in diet or the use of alcohol. With recurrent attacks the same joint may be involved or the disease may appear in a single other joint or in several joints. The periodic attacks are apt to last longer; in time, the disease may become chronic with marked joint deformity.

There are many *variations* of this fundamental typical picture. The disease may occur in women; the patient may not necessarily be healthy-looking; some other disease, such as leukemia or polycythemia, may precipitate an attack; the disease may run a chronic course from the onset; and any joint may be involved.

While there may be many different clinical pictures, *gouty arthritis should be thought of as characterized by recurrent, very acute attacks of very painful arthritis which clear up completely, leaving a normal joint between attacks early in the course of the disease*. When the patient is first seen the disease may be chronic so that the joints do not return to

normal. Here, however, the earlier history indicates the correct diagnosis. Often, acute attacks are superimposed on the chronic joint disease.

The diagnosis of gout does not depend entirely on the clinical history. Certain *laboratory procedures* help greatly: As a rule the *uric acid content* of the blood is increased. However, the uric acid is frequently higher than normal in conditions other than gout. Rarely, the gout may be active without an increase in uric acid. The *sedimentation rate* has been uniformly elevated when the disease is active. An elevated sedimentation rate is characteristic of rheumatoid arthritis also, so this finding may be only confusing. The *roentgen findings*, if typical, help greatly, but many active cases show no positive findings. The one absolute diagnostic criterion is the *presence of the tophus*. The most common site is in the margin of the lobe of the ear. A nodule should not be considered as a tophus, however, unless the needle-shaped sodium biurate crystals can be demonstrated in it.

**Incidence.**—We have analyzed our experience with gout at the Cleveland Clinic. Since January, 1930, the diagnosis of gout has been made in 135 cases (Table 1). Sixty-two of

TABLE 1  
INCIDENCE OF GOUT AT CLEVELAND CLINIC SINCE 1930

	Total cases of gout.	Cases in present series.
Total patients.....	135	62
Males.....	130 (96.3%)	59 (95.2%)
Females.....	5 (3.7%)	3 (4.8%)

the cases were studied sufficiently to warrant their inclusion in this series. In the larger group, only five, or 3.7 per cent of the patients were women. In the smaller group, three (4.9 per cent) were females.

Gout in women is rare. It is generally stated that the *incidence in women* is not over 2 or 3 per cent, although Thomson<sup>3</sup> thinks that an incidence of over 10 per cent is possible. He believes that the course of the disease in women is apt to

be more chronic and atypical than in men, and, therefore, less likely to be diagnosed. It is undoubtedly true that there are many cases of chronic arthritis in women that do not easily fit into any definite classification. The diagnosis of gout is often considered in such cases, but unless positive laboratory or roentgen evidence is available, the diagnosis should be reserved.

It is interesting to note that this disease, which we have always been prone to associate with over-indulgence, excesses of various types, sedentary occupations, and obesity, does show its greatest incidence in persons in the higher social levels. Examination of the entire series of 135 patients with gout showed that 107 of them were in the well-fed, executive, or upper-class group. Of these, fifteen were doctors. Only twenty-eight patients were found to be from the laboring group, including farmers, mechanics, day laborers, trades people and various classes of skilled workmen. However, in most instances, these individuals were found to be large, ruddy, over-nourished people.

**Obesity.**—Typically, the gouty patient is an overweight, ruddy complexioned individual who, except in acute attacks of his disease, has a definite appearance of exceptional well-being. This tendency to overweight is so striking that it has been summarized in Table 2.

TABLE 2  
INCIDENCE OF OBESITY IN 58 CASES OF GOUT

Overweight.	Number of cases.*	Per cent.
Normal—5 lbs. ....	6	9.6
5-20 lbs. ....	19	30.6
20-40 lbs. ....	11	17.7
40 lbs. and over.....	22	35.4

Average number lbs. overweight: 31.7 lbs.

Greatest amount overweight: 135.0 lbs.

\* No height or weight: 3 cases.

Underweight: 1 case (16 lbs.).

One of the patients was underweight; six were normal or less than five pounds overweight; nineteen were from 5 to 20

pounds overweight; eleven were from 20 to 40 pounds overweight; and twenty-two were 40 pounds or more overweight. A record of the height and weight was not recorded in three instances. The average number of pounds in excess of normal for the group was 31.7 pounds. The greatest amount of overweight was 135 pounds.

**Plethora.**—That the *ruddy complexion* of the gouty patient is due to plethora is shown in Table 3. It is seen that

TABLE 3  
ERYTHROCYTE COUNT AND HEMOGLOBIN IN 62 CASES OF GOUT

RBC per cu. mm. HGB Per cent	Under 4.0* Under 80%	4.0-4.5 80-85%	4.5-4.8 85-90%	4.8-5.0 90-95%	5.0-5.5 95-100%	Over 5.5 100%
No. of cases (RBC).....	3	13	15	16	12	3
No. of cases (HGB).....	6	20	8	18	6	4
Red blood cells: 31 cases—50.0%	4,800,000 or more.					
15 cases—24.2%	5,000,000 or more.					
Hemoglobin: 28 cases—45.1%	90% or more.					
4 cases—6.1%	100% or more.					
* Millions.						

50.0 per cent of the patients had a red blood cell count of 4,800,000 or more, and that 24.2 per cent had a count of 5,000,000 or more. Approximately the same holds true for the hemoglobin. It is true that these figures are not striking if compared with the red cell counts of perfectly normal, healthy persons. However, when compared with the relatively high incidence of anemia of greater or lesser degree encountered in the average clinic practice and particularly in arthritic patients, it is easy to see where the impression arises of an unusually healthy color in the patients with gout.

**Age.**—Gout is a disease of *middle life* but is, of course, not restricted to this age group. The average age of our patients at the time they were first seen was 50.5 years, with an average duration of symptoms of seven years. The onset of the disease occurred approximately between the ages of thirty-three and fifty in 60 per cent of the cases.

**Joint Involvement.**—A history of sudden, acute pain in

a great toe is important in the diagnosis of gout. However, joints other than the great toes may be the site of the initial disturbance and, if so, may mislead the examiner. When any *male* patient presents himself with a story of *acute, monarticular joint pain of sudden onset*, consideration should be given to *gout* as a possible cause even though almost any joint other than the first metatarsophalangeal is the one involved. In our series of cases (Table 4), it was interesting to find that in

TABLE 4  
FIRST JOINT AFFECTED

Joint.	Cases.
First toe.....	33
Foot.....	11
Ankle.....	6
Elbow.....	4
Shoulder.....	3
Knee.....	2
Hand.....	1
Wrist.....	1
Thumb..	1

over 25 per cent of the patients the original joint affected had been other than a great toe or the foot. After the onset of the disease, almost every other joint in the body was involved, including the temporomandibular and sternoclavicular joint in one instance.

**Hyperuricemia.**—The question of hyperuricemia in gout is fairly well established. During acute attacks, in the early stages of the disease, the level of the blood uric acid is *usually*, but not *invariably, elevated*. Therefore, with a typical history and with the type of individual in whom one might suspect gout, a diagnosis of gout need not necessarily be excluded by the finding of a blood uric acid of normal level. In the interim between attacks the uric acid will very often not be elevated. Toward the end of the first stage, years after the onset of the disease, the likelihood of finding a hyperuricemia during and between attacks increases. When the stage of *chronic* gouty arthritis is reached, the level of uric acid in the blood is almost always high.

Determinations of blood uric acid are done in the Cleveland Clinic by the *Morris-Macleod technic*<sup>4</sup> in which 2.5 mg. per cent of uric acid is the upper limit of normal.

The *average* blood uric acid in this group of sixty-two patients was 3.56 mg. per cent. The lowest value was 1.7 mg. and was found in a case where the patient's symptoms were subsiding following his first attack of acute gout five weeks previously. The highest value was 5.2 mg. per cent in a patient with acute symptoms and a history of nine years' duration with repeated attacks. An examination of Table 5 shows the

TABLE 5  
BLOOD URIC ACID IN GOUT

Uric acid, mg. per cent.	Under 2.0	2.0-2.5	2.5-3.0	3.0-3.5	3.5-4.0	4.0-4.5	4.5 plus
Number of cases.....	3	2	6	20	12	11	8
Per cent.....	4.8	3.2	9.6	32.2	19.3	17.7	12.9

Average blood uric acid: 3.56 mg. per cent.

Highest: 5.2 mg. per cent.

Lowest: 1.7 mg. per cent.

distribution of the uric acid values. A blood level of 3.0 mg. per cent or more was found in 82.2 per cent of the cases.

In an effort to demonstrate *variation in the degree of uricemia* in various stages of activity of gout, Table 6 was

TABLE 6  
ACTIVITY OF DISEASE, AVERAGE BLOOD URIC ACID, AVERAGE SEDIMENTATION RATE

	Acute.	Acute subsiding.	Chronic progressive.	Chronic.	Inactive.
Number of Cases.....	28	10	1	5	6
Per cent.....	56.0	20.0	2.0	10.0	12.0
Average blood uric acid....	3.6	3.0	3.0	4.0	3.7
Average sedimentation rate..	1.16	.92	1.26	.80	.86

prepared. Cases were classified under the headings of "acute," "acute subsiding," "chronic progressive," "chronic," and "inactive" gout. As would be expected, the average level of uric acid in the blood in the acute subsiding group is lower than in

the acute group. The relatively low value found in the chronic progressive group is not significant since only two cases are represented. The high value for blood uric acid seen in chronic gout is exactly what one might expect. In the inactive group a surprisingly high average value was found. The occurrence of this is probably best explained on a basis of long duration of the disease and numerous acute attacks, although when first observed by us the cases were inactive. The average duration of the disease in this group was 10.7 years, with an average of thirteen acute attacks.

**Tophi.**—Authorities agree that there is only one specific lesion of gout, namely the tophus. A diagnosis of the condition before the appearance of tophi is often easily made but should be qualified by the designation *presumptive* or *pretophaceous gout*. Following the appearance of tophi, a diagnosis of *proved* or *tophaceous gout* may be applied. As hyperuricemia develops and as the disease becomes more chronic, the possibility of demonstrating tophi is increased. However, the presence of tophi is an extremely *variable* finding. They are not as commonly found as is generally suspected. Furthermore, they may appear during any stage of the disease, with or without a chronic hyperuricemia, and often may not appear at all although the disease may be of twenty or thirty years' duration and although the blood uric acid may be decidedly high.

Table 7 shows that there were only fourteen cases in this series in which tophi could be demonstrated. The duration of

TABLE 7  
INCIDENCE OF TOPHI

Number of cases.	Duration of symptoms.	Blood uric acid, mg. per cent.	x-ray.
14	Longest—10 years	Highest—5.2	Negative 8
(22.5%)	Shortest—2 weeks	Lowest—2.8	Positive 5
	Average—5.5 years	Average—4.07	None 1

No tophi in 13 cases of 10–30 years' duration, with average blood uric acid of 3.5 mg. per cent.

symptoms in these patients ranged from only two weeks to ten years. The patient with symptoms of only two weeks'

duration must have had gout for a longer period of time than the history would indicate. The fact that tophi developed before the onset of joint symptoms is no more difficult to understand than the symptom-free interval between acute attacks which the patients typically show. No tophi were found in thirteen cases with histories of from ten to thirty years' duration. The average level of uric acid for the group with tophi was 4.07 mg. per cent, with a spread of 2.8 to 5.2 mg. per cent. This further demonstrates the fact that *proved, tophaceous gout may be present with a blood uric acid of normal level.*

**x-Ray Findings.**—Positive roentgen evidence of gout is *usually lacking in early attacks.* This is often disappointing since the symptoms and clinical findings are so striking. Hench<sup>2</sup> believes that a deposition of urate probably occurs in the points in every attack, but that these areas are too small to be visualized early in the disease. As the disease progresses, the possibility of positive findings by roentgen examination increases. Strangely enough, however, many cases show nothing by x-ray although the disease may have been present for several years and although there may have been repeated attacks of severe joint pain and swelling. When deformity results in the stage of permanent arthritis, roentgen changes are always present but may not have the so-called typical appearance of gout.

TABLE 8  
x-RAY FINDINGS

x-Ray.	Number of cases.	Per cent.	Average duration of symptoms, years.	Average blood uric acid mg. per cent.
Positive . . . . .	19	30.6	5.70	3.6
Negative . . . . .	33	53.2	8.70	3.6
Not done. . . . .	10	20.0	. . .	. . .

Earliest positive x-ray: 2 months.

3 cases of 25 years and 1 of 30 years' duration were negative by x-ray.

*Positive roentgen evidence of gout was found in only nineteen of the cases as shown in Table 8. The average duration*

of symptoms and the average level of the blood uric acid was 5.7 years and 3.6 mg. per cent, respectively. The patient with the earliest positive roentgen findings was seen two months after the onset of symptoms. Three cases of twenty-five years' duration and one of thirty years' duration were negative by roentgen examination.

Of the fourteen patients with tophi, five were found to have demonstrable bone changes (Table 7).

*Areas of erosion* representing osseous tophi in articular or juxta-articular bone constitute the typical appearance of gout by x-ray. These may appear as *destructive changes* in articular surfaces or may show up as definite *punched-out areas* in the shaft of the bone. Often these areas are small and very similar to the changes found in degenerative or atrophic arthritis. Unless areas of erosion of this type are large, they cannot be directly attributed to gout but, if large, they are highly significant. However, it is apparent from the above data that *roentgen evidence of gout*, like the appearance of tophi and the finding of hyperuricemia, is *variable* and *unreliable*, especially during the early stages before chronic arthritic changes develop.

**Conditions Associated with Gout.**—Tissues other than the joints are affected in gout, notably the kidneys. Schnietker and Richter<sup>5</sup> found a vascular *nephritis* in 31 per cent of fifty-five cases of this disease. Although a faint to heavy trace of albumin was found in the urine of about half of our patients, sufficient indication to warrant a study of kidney function was lacking. Only three patients had casts in the urine.

*Renal stones* are not uncommon in gout. Although only seven, or 11.0 per cent, of our patients had or gave a history of stone, a useful rule to follow as suggested by Hench<sup>2</sup> is "suspect gout in acute or chronic arthritis with a history or findings of renal colic or nephritis." This may be helpful at times in differentiating between rheumatoid arthritis and gout.

*Bursitis or tendinitis* may often be attributed to gout, but the proof of this depends upon the finding of other manifestations of the disease. Debris removed from affected bursae is

almost uniformly nonuratic in nature. In one case in this series large, bilateral olecranon bursae were found in a man who had a typical history of gout and a blood uric acid of 3.5 mg. per cent. Hard, gritty material could easily be palpated in the bursae, but aspiration revealed no sodium biurate crystals.

Vague symptoms from the *gastro-intestinal tract*, attributed by some to gout, are extremely indefinite. These symptoms are probably reflex in origin from the kidneys.

**Sedimentation Rate.**—A laboratory study of exceeding interest and a valuable aid to diagnosis in certain cases is the determination of the sedimentation rate. Only a few reports relative to the effect of gout on the sedimentation of erythrocytes have appeared in the literature and these represent study of small series and scattered cases. Kahlmeter<sup>6</sup> has reported six cases of gout, in all of which the rate was elevated, the more clinically active cases showing the greatest rise. It is seen from Table 9 that 85 per cent of the cases showed a rate of

TABLE 9  
SEDIMENTATION RATE IN GOUT

Sedimentation rate, in mm. per min.	Under 0.45	0.46-0.60	0.6-0.8	0.8-1.0	Over 1.0
Number of cases.....	9	7	9	8	29
Per cent.....	14.5	11.3	14.5	12.9	46.7

Average sedimentation rate: 1.00 mm. per min.

Highest: 2.00 mm. per min.

Lowest: 0.25 mm. per min.

0.46 mm. per minute or more. The average was 1.0 mm. per minute. The highest was 2.00 mm. per minute. The lowest rate was 0.25 mm. per minute and was found in an inactive case. The sedimentation rate was determined by the method described by *Rourke and Ernstene*.<sup>7</sup> A rate of 0.45 mm. per minute is the upper limit of normal by this method. Reference to Table 6 shows that the sedimentation rate *varies with the clinical activity of the disease*. These findings are essentially what one would expect.

An explanation of this elevation in the sedimentation rate is not evident at the present time. Certainly it is not due to infection, for careful survey of these individuals for chronic foci has usually proved unsuccessful. Where chronically infected teeth, tonsils, sinuses, or prostates have been found and removed or treated, as was the case in over 50 per cent of these cases, the course of the disease has not been affected and the sedimentation rate has continued to be elevated. Since it has been shown quite definitely by Gilligan and Ernstene<sup>8</sup> that the plasma fibrinogen level is the major factor in controlling the sedimentation rate, it may be assumed that, in gout, the plasma fibrinogen has become elevated, due, perhaps, to toxic or otherwise irritating substances liberated because of faulty protein metabolism. Or, perhaps, there is faulty liver function, with resultant impairment of protein metabolism producing an increase in the plasma fibrinogen.

It has been suggested by some that there is a functional disturbance of the liver in gout. It would not appear from an examination of Table 6 that there were any close parallelism between the blood uric acid, which reflects in part at least the extent of metabolic dysfunction, and the sedimentation rate.

**Summary.**—Gout is not as uncommon a disease as is generally believed. It typically appears in obese, healthy looking, middle-aged men engaged in sedentary occupations. Characteristically, it is acute in onset, usually involving a single joint, most commonly the great toe or the foot. It runs a chronic course, with irregular remissions and exacerbations of the joint symptoms and usually with eventual multiple joint involvement.

Too much dependence for diagnosis should not be placed upon the presence of a hyperuricemia; although the blood uric acid is frequently elevated above normal limits, it is not invariably so. Similarly, too, much dependence should not be placed upon the finding of tophi or positive roentgen evidence of gout, since these pathognomonic phenomena are often lacking even in cases of long duration.

A laboratory test of decided value in establishing the diag-

nosis of gout is the sedimentation rate. This rate was found to be above normal in 85 per cent of the sixty-two cases studied in this series. This laboratory procedure may prove valuable in the differential diagnosis of gout, osteo-arthritis, traumatic arthritis, periartthritis, tendinitis and fibrositis. It would not aid materially in differentiating between gout and rheumatoid arthritis.

It would appear from this review that, in the final analysis, the diagnosis of gout depends primarily upon a careful *clinical evaluation* of the problem, since positive laboratory evidence is often lacking and therefore unreliable.

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## THE TREATMENT OF POSTOPERATIVE PARATHYROID TETANY: USE OF DIHYDROTACHYSTEROL (A.T. 10)

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Of the various etiologic types of adult tetany, including those due to alkalosis, pregnancy and lactation, renal failure, steatorrhea, administration of neutral or alkaline phosphates, and hypoparathyroidism, the latter, following thyroidectomy, is probably most often encountered as a therapeutic problem. The incidence of this postoperative complication has decreased materially as surgical technic has improved. However, a certain number of cases are unavoidable, particularly in operations for *recurrent hyperthyroidism*. The condition is seen after operation about twenty-five times more frequently in women than in men, which is interesting in view of the fact that thyroidectomy is performed approximately four times more often in women.<sup>1</sup>

**Symptoms.**—The symptoms of postoperative parathyroid tetany, particularly *acroparesthesias*, *hyperesthesias*, *muscle pain* and *contraction*, *convulsions*, and the subsequent *trophic changes* affecting the optic lenses, hair, skin, nails, and teeth are too well known to require further elaboration. Various signs, of which *Erb's*, *Chvostek's*, and *Trousseau's* are probably the most dependable (the latter two being simpler and more commonly used), are helpful in diagnosis of the latent form. The *serum calcium* is probably depressed in all untreated cases of true parathyroid tetany, although it will occasionally not fall below the lower limit of normal, 9 mg. per 100 cc. *Serum phosphates*, in our experience, are always elevated. If a calcium level of 10 mg. per 100 cc. or higher is

found in the presence of symptoms, some accessory factor, such as hyperpneic or idiopathic tetany, should be suspected.

### TREATMENT

**Acute Parathyroid Tetany.**—The treatment of acute tetany, which usually appears one to five days after operation, should be initiated as soon as the diagnosis is made. Large quantities of calcium, orally, are of fundamental importance. For this purpose, *calcium lactate*, preferably dissolved in warm water and later cooled, is inexpensive and efficacious. Chemically pure *calcium carbonate* may be substituted if the former drug is not well tolerated. *Calcium gluconate* may be used, but it is less desirable because of its relatively low calcium content. All calcium compounds containing *phosphates* should be rigidly avoided. The *dosage* depends upon the severity of the condition and therapeutic response, but in a majority of instances it may average three teaspoonfuls three or four times a day.

*Intravenous* calcium will effectively ameliorate symptoms in severe or convulsive episodes in either the acute or chronic phase of the disease. Ten to 20 cc. of 10 per cent calcium gluconate may be injected slowly. Calcium chloride is even more effective, but it is potentially dangerous because of its severely irritating and necrotizing effect upon the subcutaneous tissue and veins. For this reason it is probably wiser to use 10 to 20 cc. of a 3 to 5 per cent solution, injected slowly and cautiously, or preferably given intravenously by the gravity method, preceded and followed by normal saline.

*Parathyroid extract* is of proved value in acute cases, and can be used in conjunction with oral calcium as outlined above when the latter is not sufficient. Doses of 50 to 100 units twice daily are usually adequate. The unlikely possibility of a resultant hypercalcemia must be kept in mind.

Progress should be followed by frequent *serum calcium* and *phosphate determinations* and by careful *clinical observation*. With the disappearance of symptoms, therapy can usually be withdrawn slowly after seven to fourteen days to determine

whether the condition has subsided after temporary damage to the parathyroids, or whether it is entering a chronic phase. The majority of patients either recover promptly or proceed to a life-long chronic state. A small percentage may recover completely after many months.

**Chronic Parathyroid Tetany.**—The management of chronic parathyroid tetany is undertaken with two objectives: *symptomatic comfort* of the patient, and *prevention* of later trophic changes. Both can be successfully accomplished with maintenance of the patient in a state of comparative normality. It is important that *serum calcium* and *phosphate determinations* be done at intervals of a few months. The reason for this is prevention of subsequent trophic alterations. Certain patients develop a relative insensitivity to milder symptoms so that they may appear symptom-free in the presence of distinctly altered blood chemistry.

Large quantities of *oral calcium* are fundamentally important and may be used for years in the doses outlined for treatment of acute tetany. Modifications may be made, based upon the patient's progress and serum calcium and phosphate levels. A certain number of patients will respond satisfactorily without resorting to supplementary therapy. However, in many instances, *other measures* are necessary. It should be emphasized, however, that such measures are merely adjuncts to treatment, and that oral calcium in large doses is still basically important.

The efficacy of *vitamin D* has been emphasized by Boothby and Davis.<sup>2</sup> The primary action is the promotion of increased calcium absorption. Relatively large doses are required, as much as 5 to 10 cc. of cod liver oil three times a day. Synthetic preparations, such as *viosterol*, may be used, but the dosage must be carefully regulated. If large doses of vitamin D are used, the possibility of *hypervitaminosis D* with attendant organic calcification must be kept in mind and the progress followed carefully. This is particularly true if parathyroid extract is given concurrently. In our experience, vitamin D in moderate dosage has been a helpful agent in some cases, but

has not been considered of sufficient importance to warrant exclusive use. Regulated sunbathing or artificial ultraviolet irradiation are beneficial for the same reason, and may be used in conjunction with other therapy in practically all cases.

*Parathyroid extract* may be administered over long periods of time, provided oral calcium is given concurrently. By so doing, we have not observed any apparent development of intolerance to the preparation, as reported by a number of others; nor have we noted any significant osseous decalcification. The dosage varies widely, dependent upon individual requirements, but will probably average 50–100 units daily or every other day. It thus becomes a fairly expensive agent.

Various sugars, particularly *lactose*, act to lower the level of serum phosphates, and may be given with oral calcium in equal dosage when indicated. A diet of low phosphate content is helpful in either acute or chronic parathyroid tetany, although it is not always required. Any postoperative *hypothyroidism* should be corrected because of the effect of the thyroid on calcium metabolism.

Until recently, *parathyroid transplants* were only of transient value. The alteration in technic advocated by Stone<sup>3</sup> may lead to better results.

By various combinations of these measures, patients treated at the Clinic over periods of years have been maintained in a fair degree of comfort, and have avoided trophic changes unless they were careless in following the prescribed treatment. However, intermittent mild *paresthesias* have not been uncommon, and occasional acute exacerbations have occurred. Results of treatment with dihydrotachysterol (or A.T. 10) have been quite favorable by contrast.

**Dihydrotachysterol (A.T. 10).**—Dihydrotachysterol was converted from tachysterin, a derivative of irradiated ergosterol, as a result of the researches of Holtz, Gissel and Rossman.<sup>4</sup> It is marketed as a 0.5 per cent solution in oil of sesame and is administered orally. It has been used extensively in Europe, but only moderately so in this country, and has been very effective. Its action, as described by Albright et al.,<sup>5</sup>

simulates more closely that of parathyroid extract than of vitamin D.

McCullagh and Ryan,<sup>6</sup> among others, have recently studied its action by clinical observation and laboratory investigation. The following conclusions were reached:

Any case of *chronic parathyroid tetany* which fails to respond satisfactorily to large doses of oral calcium alone may be treated by A.T. 10 as a supplementary measure. Calcium by mouth should be continued, although a somewhat smaller dosage may be used in certain instances. Frequent *serum calcium and phosphate determinations are important* during the establishment of a maintenance dose, since the drug is apparently cumulative in its action and can produce dangerously high levels of hypercalcemia. In addition, individual response to A.T. 10 is variable. For these reasons, we feel that the *dose*, in mild or moderately severe tetany during the period of initial regulation, should usually *not exceed 2 cc. per day*. In *severe tetany*, it is probably wiser to elevate the serum calcium by other means, and begin with relatively small doses. The majority of cases will later be satisfactorily maintained on 0.5 to 0.75 cc. daily or every other day, always *in conjunction* with oral calcium. By observing these precautions, the danger of untoward effects is minimized. The results in several cases have surpassed those obtained by any other method of treatment, and symptomatic improvement has been observed prior to any measurable shift in serum calcium or phosphates.

*Illustrative Case.*—One case, reported previously,<sup>6</sup> is briefly summarized to illustrate the effect of this drug:

A twenty-seven-year-old woman developed tetany after thyroidectomy fourteen years ago, and came under observation at the Clinic in January, 1937. Treatment had included parathyroid extract in an average dosage of 50 units every other day, and calcium lactate, 24 to 32 gm. daily. She had progressed fairly well symptomatically, but serum calcium and phosphates were rarely normal, averaging about 7.5 and 5.5 mg. per 100 cc., respectively, on numerous visits. In March, 1939, she gave a history of severe upper respiratory infection

two weeks before followed by marked symptoms of tetany (Fig. 59).

The serum calcium was 4.3 mg. and serum phosphates 6.6 mg. per 100 cc. Calcium lactate was increased to 48 gm. daily, where it was maintained. Parathyroid extract was continued, and she received 100 units every other day for six doses. A.T. 10, 1 cc. daily, was begun on the eighth day of observation and was ultimately established at a maintenance level of 0.3 cc. daily. The serum calcium rise, which began under the

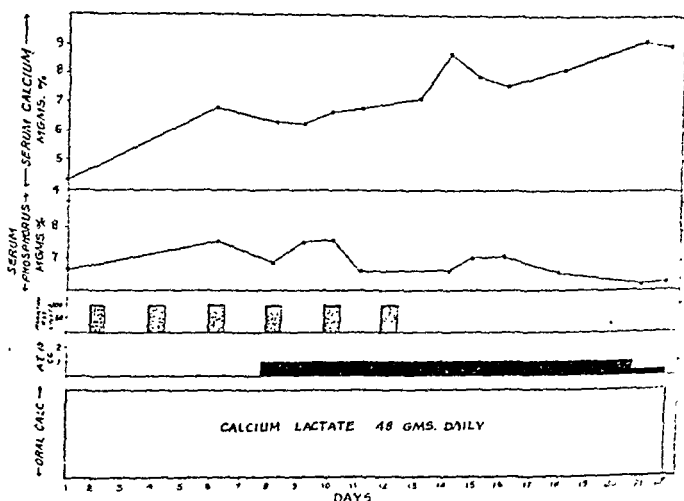


Fig. 59.

increased calcium lactate dosage, was accelerated by the addition of A.T. 10, and continued after parathyroid extract was discontinued. Serum phosphates fell moderately. Symptoms of tetany disappeared before A.T. 10 was started, and Trousseau's and Chvostek's signs became negative soon afterward. The patient has been maintained satisfactorily on these measures for a period of months.

A.T. 10 has been used successfully in the treatment of *acute postoperative tetany*. We have hesitated to employ it, however, because of the large doses required with the attendant

danger of cumulative action and hypercalcemia, particularly in view of the fact that spontaneous improvement in the patient's condition cannot be well evaluated.

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## THE DIFFERENTIATION OF THE OBSCURE ANEMIAS

RUSSELL L. HADEN

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Not infrequently the clinician sees a patient with a marked anemia for which there is no apparent cause. Almost always, however, the etiology can be discovered if the clinical and laboratory study is thorough. The more important causes for a cryptic anemia are:

1. Pernicious anemia.
2. Leukemia or other bone marrow disease, such as myelomatosis.
3. Chronic nephritis or some other intoxication, such as lead poisoning or Hodgkin's disease.
4. Chronic blood loss, or unsatisfied iron need for growth or pregnancy.
5. Malignancy, especially of the stomach and cecum.
6. Idiopathic hypochromic anemia.
7. Idiopathic aplastic anemia.

To study an obscure anemia, taking a *good history* is most important, especially in relation to *chronic bleeding*. A woman may have a menorrhagia with excessive blood loss which she does not realize is abnormal. An earlier history of renal disease may give a clue to impaired renal function. The history of pernicious anemia is usually typical. Difficulty in swallowing and thin, spooned nails at once suggest idiopathic hypochromic anemia.

The following *laboratory examinations*, together with the history, will usually afford sufficient data for a correct diagnosis. The tests are simple and often all must be done in a puzzling case:

1. Complete blood study, including hematocrit reading, reticulocyte count and icterus index.

2. Gastric analysis.
3. Test of feces for occult blood.
4. Concentration preparations of leukocytes if a leukopenia is found.
5. Urea clearance test of renal function.
6. Bone marrow puncture.
7. Radiographs of stomach and colon.
8. Radiographs of skull and ribs.

**Pernicious Anemia.**—The anemia in pernicious anemia may be most marked and the cause never be evident. We now know the disease is due to a lack of a normal gastric secretion by which a substance necessary for the maturation of erythrocytes is formed. The blood always shows a macrocytosis of the red cells, so the *volume index* is regularly above normal and usually high. A macrocytosis may, however, be due to a high reticulocyte count, which is never found in untreated pernicious anemia; to deficiency disease such as sprue; to liver disease; to aplastic anemia, or to other diseases of the marrow. The absence of a macrocytosis almost excludes active pernicious anemia. The *test meal* always shows an achlorhydria and a low total acidity. A combination of *achlorhydria* and a *macrocytic anemia* are almost pathognomonic of pernicious anemia.

The clinical study will usually show a clean, smooth tongue with a history of *glossitis*, and impaired vibratory sense with a history of *numbness* and *tingling* of the hands and feet. A coated tongue and a positive test for free hydrochloric acid absolutely rule out the disease.

Pernicious anemia should be the first to be identified or excluded in studying a cryptic anemia. All too often, however, an anemia due to some other cause, such as *nephritis* or *leukemia*, is treated as pernicious anemia. The anemia of congenital *hemolytic icterus* may be confused with pernicious anemia. Here, however, the cells are decreased in diameter and increased in thickness. The reticulocyte count is high; the fragility is increased; jaundice and splenomegaly are almost always present. The final proof of the correctness of a

diagnosis of pernicious anemia is a *specific response to liver therapy*.

**Leukemia.**—Anemia is almost an *invariable symptom* of leukemia of every type when the disease is well developed. Very early in the course of the disease anemia may be absent. If the leukemia is evident from the clinical findings and physical examination, the reason for the anemia is evident. In about a fourth of the cases of leukemia there is no leukocytosis; often there is a leukopenia. Without a leukocytosis, the abnormal immature cells are usually few in number and are often hard to find in the blood film made in the usual manner.

Even without finding abnormal cells in the blood, one might suspect leukemia from the presence of an *enlarged spleen*. If the reason for the splenomegaly is not evident, the spleen should always be *irradiated* as a *diagnostic* measure. If the splenomegaly disappears or the spleen becomes smaller after irradiation, the enlargement must be due to leukemia, Hodgkin's disease, or lymphoid hyperplasia. An enlarged spleen does not respond to irradiation if it is due to Banti's disease, cirrhosis of the liver, syphilis, malaria, or to many other causes which may produce a splenomegaly.

Usually, however, the blood study alone enables one to make the correct diagnosis if *concentration preparations of the leukocytes* are available. In making such a preparation, an oxalated specimen of blood is allowed to stand for a few minutes until the red cells have settled out. The specimen is then centrifuged and film preparations are made from the "buffy" coat or surface layer of cells where the leukocytes and platelets are concentrated. In this preparation many leukocytes are available for study. As a rule, the red cells in an anemia due to leukemia tend to be macrocytic. A *bone marrow puncture* is simply done and may help greatly in making the diagnosis of leukemia.

Two other types of bone marrow disease may cause a marked anemia. These are *Hodgkin's disease* and *myelomatosis*. As a rule, the anemia of Hodgkin's disease is due to toxic depression of marrow activity incident to the general

toxemia of the disease. It may, however, be due in some cases to actual invasion of the marrow by the disease. The diagnosis here is difficult to make. The almost constant anemia of myelomatosis is usually puzzling. Radiographs may not show any changes until late in the course of the disease. Often there are never any typical "punched out" areas in the skull and other bones. Here the presence of *Bence-Jones protein* in the urine or blood may make the diagnosis, although this is absent if the myelomatosis is due to overgrowth of cells other than plasma cells. If myelomatosis is suspected, a marrow puncture should always be done, as the finding alone of a hyperplasia due to plasma cells establishes the diagnosis. Extensive metastatic malignancy of the bone marrow will also produce an anemia.

**Chronic Nephritis.**—Perhaps the most commonly overlooked cause of obscure anemia is chronic nephritis. Almost every patient with a significant nephritis has some degree of anemia. This is true in pyelonephritis as well as glomerular or arteriosclerotic renal disease. The anemia often parallels the severity of the disease. Every patient with an unexplained anemia should have the *renal function* studied, with a *urea clearance test*. In the obscure case the signs of kidney disease may be minimal or even absent. Thus, little may be found on examination of the urine and the blood pressure may not be elevated, so there is little to incriminate the kidneys.

The anemia of kidney disease is probably due to a toxic and depressant action of retained metabolic products on the marrow. These products seem to act just as other known toxic products such as lead do. With *lead poisoning*, the constant punctate basophilia suggests this disease. *Infection*, *Hodgkin's disease* and other *toxic* clinical states may act similarly to chronic kidney disease.

The anemia of nephritis and other toxic states is usually normocytic and normochromic so that volume and color indices are within normal limits. An *impaired kidney function* can be demonstrated if the anemia is due to nephritis. Response to treatment is most unsatisfactory since little can be done to eliminate the cause of the anemia.

**Chronic Loss of Blood.**—A chronic blood loss may go on for a long time without being evident or suspected. Thus, bleeding from *hemorrhoids* may pass unobserved; a woman may lose much more blood during *menstruation* than the history indicates; occult bleeding from a *silent lesion in the gastro-intestinal tract* is not uncommon.

The anemia of chronic blood loss is due to a deficiency of iron for the formation of hemoglobin, as the loss of blood means the loss of iron. A similar picture is presented if there are normal demands for iron beyond the normal supply. With rapid growth, the store of hemoglobin and of iron should increase greatly unless iron is deficient. With a deficiency of iron, the blood picture is that of chronic blood loss.

The *blood picture* in an anemia due to chronic blood loss or other iron deficiencies is very typical. There is always a *low color index* and, if this continues, the *volume index* becomes low also. The *hemoglobin* is thus reduced out of all proportion to the reduction in number of red cells. Often the *red blood cell count* is even above normal. With such blood findings, chronic bleeding must always be considered as a possible cause of the anemia. The history of some abnormal blood loss must be sought for; the *stools* must always be tested for occult blood. The response to adequate *iron therapy* here is most gratifying.

**Malignancy.**—Anemia is almost a *constant accompaniment* of malignancy. As a rule, the primary lesion is evident so the anemia does not seem any more than one would expect. Malignancy of the stomach and of the cecum and ascending colon may produce an anemia out of all proportion to the size and symptoms of the tumor and so be unrecognized. There may be some blood loss with ulceration in such tumors, but bleeding does not explain fully the anemia. The anemia may be marked without finding even a positive test for occult blood. If thought of and searched for, however, such lesions will usually be found.

The blood picture in *carcinoma of the cecum and ascending colon* is almost always that of a marked hypochromic and

microcytic anemia. The findings are thus identical with those of an anemia due to chronic blood loss. *Malignancy of the stomach* may produce a macrocytic, normocytic, or hypochromic anemia. Here the stools should always be examined for blood. The radiographs of colon and stomach nearly always reveal the lesion responsible for anemia.

**Idiopathic Hypochromic Anemia.**—In idiopathic hypochromic anemia, the anemia is usually *extreme* and without evident cause. The patient is usually more anemic than one would expect from her appearance. Often the anemia will continue for years before it is properly treated. Many patients have an *achlorhydria*, so the condition is often diagnosed and treated as pernicious anemia.

Idiopathic hypochromic anemia occurs almost entirely in *women*. The *sclerae* are blue if the anemia is marked; the *tongue* is often atrophic and painful; the *finger nails* are usually paper thin, and often flattened or even spoon-shaped (*koilonychia*). Often there is a coincident *neuritis* due to an accompanying vitamin B deficiency.

The cause of idiopathic hypochromic anemia is not clear. The *blood picture* is typical of that of an iron deficiency anemia, since the color index is always low and the volume index usually low. Most women who have the condition have had some abnormal *blood loss* usually by menorrhagia, although this is not always evident. It seems probable that in addition to the blood loss, there is impaired absorption of iron in the duodenum, probably secondary to the achlorhydria. It is possible there is also some disturbance in the utilization of iron. With adequate *iron medication*, the blood will return to normal, although it is often necessary to give some iron all the time to prevent a recurrence of the anemia.

The *clinical picture*, the *blood findings*, the *exclusion* of other causes or an *iron deficiency* and the specific response to iron therapy, should make the diagnosis.

**Idiopathic Aplastic Anemia.**—True idiopathic aplastic anemia is a very uncommon disease. It is probably the rarest of all the recognized types of anemia. Most cases of so-called

aplastic anemia are due to leukemia, or other bone marrow disease, to pernicious anemia, to nephritis, or to malignancy.

In aplastic anemia, as the name indicates, the *marrow* is *empty* and *yellow*, due to replacement of the normal red marrow by fatty tissue in the ribs and the sternum. The aplasia involves all elements of the marrow, so there is usually a *leukopenia* and *thrombopenia* as well as the anemia. The reduction in hemoglobin and erythrocytes is progressive and very chronic. The red cells often show a slight macrocytosis so that the *volume index* is commonly above 1.00. *Reticulocytes* are absent or greatly reduced.

The final diagnosis rests on the demonstration of an aplastic marrow by *marrow biopsy* or *puncture*. The disease should be suspected when all other cases for a cryptic anemia are excluded. There is no characteristic clinical picture, nor any satisfactory response to treatment.

**Illustrative Cases.**—The following cases are cited as typical examples of cryptic anemia:

*Case 1.*—*Anemia due to symptomless carcinoma of the stomach.*—A housewife, age sixty-four, was admitted to the Cleveland Clinic complaining of weakness. She stated that she had noticed some weakness for six years. For eight months this symptom had been marked. She complained also of numbness of the hands and feet and of a "scalded" tongue. Three months before admission, a blood count showed a marked anemia, so she was advised to eat liver and was given 12 capsules of liver extract daily. She had noted some palpitation and edema of the feet, and had lost 20 pounds in weight. There had been no digestive symptoms.

On examination the patient was 25 pounds above the normal average for her age and height. No abnormality was noted in the heart, lungs, or abdomen. The reflexes were active and the vibratory sense intact. The tongue was coated.

The blood count showed: red cells, 2,910,000; hemoglobin 42 per cent (6.5 gm.); volume index, 0.95; color index, 0.73; white cells, 10,750; a normal differential count; reticulocytes,

3.3 per cent, and icterus index, 2 units. The urine was negative, the stool contained occult blood, and the test meal showed 18 degrees free acid, and 29 degrees total acid.

A roentgenogram of the stomach showed a large polypoid carcinoma at the pylorus with 60 per cent retention of barium in five hours.

The pyloric end of the stomach was resected and the preoperative diagnosis of adenocarcinoma verified by histologic examination. No metastases were found in the lymph glands. The recovery from the operation was uneventful.

The patient was next seen six and a half years later for an acute glaucoma requiring enucleation of the eye. Her digestive and general health had been excellent before the onset of the eye trouble. Her weight was 123 pounds. A roentgenogram of the stomach showed no evidence of ulcer or cancer. A fractional test meal showed no free acid in any specimen. The blood count showed 4,520,000 red cells and 74 per cent (11.5 gm.) hemoglobin.

*Comment.*—This patient had no symptoms suggesting disease of the stomach, but the stool showed occult blood, indicating blood loss somewhere in the gastro-intestinal tract. She had evidently been treated three months for pernicious anemia without improvement. The coated tongue, the absence of macrocytosis of the red cells, the intact vibratory sense, and the presence of free hydrochloric acid in the gastric contents ruled out pernicious anemia in spite of the unexplained anemia and the history of glossitis and paresthesias. The correct diagnosis was made by roentgen ray. The long period (six and a half years) of good health and the negative roentgen findings indicate that she was permanently cured by operation.

*Case II.*—*Anemia due to chronic nephritis simulating pernicious anemia.*—A housewife, aged fifty-one, complained of weakness and headache. She stated that she had been weak and short of breath for years, and had been confined to bed for six weeks. Recently she had been vomiting and had noticed some edema of the ankles. Her appetite was poor. She had

stopped menstruating seven years before, but during the week preceding admission she had had a uterine hemorrhage requiring packing. She had lost 20 pounds in weight and had had abdominal cramps.

On examination she was still 25 pounds underweight. The general examination was negative except for slight edema of the ankles and a loud precordial systolic murmur. There were no neurologic signs or symptoms. The blood pressure was 232/120. The pelvis was negative.

The blood examination showed red blood cells, 1,650,000; hemoglobin, 21 per cent (3.25 gm.); volume index, 1.00; color index, 0.73; reticulocytes, 3.2 per cent; icterus index, 3 units; white cells, 6,300, and a normal differential count. The urine showed pus, a trace to 1+ albumin, and specific gravity 1.010 to 1.018. No casts were found. The test meal showed no free acid and a total acidity of 26 degrees. The urea clearance test was 20 per cent of normal, with a blood urea of 156 mg. per 100 cc.

*Comment.*—This patient had been diagnosed and treated as having pernicious anemia. There was an achlorhydria, but the combined acidity was relatively high. In pernicious anemia, with the absence of free hydrochloric acid, there is almost always a very low total acidity. The red cells showed no macrocytosis and the blood pressure was high. The true findings above were not diagnostic of kidney disease. The high blood urea and the urea clearance within the uremic level completed the diagnosis of uremia, which was the evident explanation for the anemia.

*Case III.—Anemia due to plasma cell myelomatosis.*—A man, aged sixty, had been very weak for five months. Three months after the onset of symptoms, he was found to have a macrocytic anemia and was treated with liver and iron, without improvement. Several transfusions had been given. The physical examination throughout the patient's illness had been negative. The weakness became so severe the patient was confined to bed and the anemia became more marked. Just

before he was seen in consultation, agglutination of the red cells on diluting with Hayem's solution was noted. This suggested the diagnosis of myelomatosis, so roentgenograms of the ribs, spine and skull were taken. The only positive findings were some suggestive areas of rarefaction in the skull. No typical "punched-out" areas were seen.

The blood taken when the patient was seen in consultation showed the following: red blood cells, 1,340,000; hemoglobin, 37 per cent (5.7 gm.); volume index, 1.6, and color index 1.37. The total serum proteins were 10.9 gm., the albumin being 2.7 gm. and the globulin 8.2 gm. per 100 cc. The blood urea was 147 mg. Bence-Jones protein was demonstrated in the urine. A marrow puncture showed only many plasma cells. The patient died three weeks later.

*Comment.*—The anemia here was extreme and macrocytic, suggesting pernicious anemia. The red cells in an anemia due to bone marrow disease are often macrocytic. The lack of response to liver therapy excluded pernicious anemia. The diagnosis of myelomatosis was suggested by the auto-agglutination of the red cells, the Bence-Jones protein in the urine, and the high blood serum proteins. The diagnosis was made definite by finding the marrow filled with plasma cells. The anemia here is due to the overgrowth of plasma cells within the marrow spaces, thus crowding out the red cells and producing the anemia.

In *myelomatosis*, the kidney is usually infiltrated by the plasma cells and the tubules are occluded, probably by the Bence-Jones protein. This explains the urea retention and the renal insufficiency which here intensified the anemia.

## THE DIAGNOSIS OF BASAL TUBERCULOSIS

H. S. VAN ORDSTRAND

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THE diagnosis of tuberculosis limited to the lower lung fields is usually fraught with difficulties. Fortunately, owing to the many interesting diseases to be differentiated in this region of the body, this entity challenges the clinician. Basal lesions are the most confusing of all pathologic conditions which may occur in the chest because of their site of drainage from the upper respiratory tract. Bronchiectasis, lung abscess, lung tumors, foreign bodies, fusospirochetal disease, pulmonary mycosis, and the many nontuberculosis pneumonias must be considered in exclusion, as well as many of the rarer conditions. As there is no typical roentgen picture of tuberculous infiltration, and since its symptoms and signs are similar to those of many other diseases in the lower lung fields, the diagnosis can be accurately made only by finding *Koch's acid-fast bacillus*. It may be inferred in the absence of the specific organism, and this by careful exclusion of the above mentioned diseases. It is the purpose of this paper to clarify some of the diagnostic confusion in basal chest lesions with reports on two unusual cases of this type of tuberculosis.

Because of the varied symptomatology, basal tuberculosis has not infrequently been missed. On the other hand, nontuberculous diseases have occasionally borne this diagnosis. Some cases have been relatively asymptomatic. In other cases the pleural pain may simulate that of lung tumor, the fever that of many febrile diseases, the copious sputum notable of bronchiectasis, etc. As in apical tuberculosis, the *case history* yields far less of value toward the final diagnosis than in most

diseases. It has been computed by some to be less than a 10 per cent aid toward the final conclusion. A past history of *pleural effusion* is of much value, as in tuberculous infection of the upper pulmonary tissue. *Hemoptysis* is of less importance in contrast. The relative frequency of hemoptysis in bronchiectasis over the acid-fast disease is well known, particularly with the basal form of the latter.

The roentgenologist is handicapped in being able to make a definite diagnosis of basal tuberculosis by the fact that the *tubercles do not have a characteristic roentgen-ray shadow*. In contrast to his 90 per cent chance of being right in apical infiltrations, he has only a 5 per cent chance in unilateral lower lung lesions and no more than 10 per cent chance in bilateral lower lung lesions. The roentgen evidence of a disease process in this location, therefore, necessarily entails further laboratory work, and often the aid of the *bronchoscopist*, in arriving at the correct diagnosis.

**Differential Diagnosis.**—As the site of predilection of most nontuberculous pulmonary diseases is in the lower lung tissues, the common, as well as many of the rare, respiratory diseases must be considered in *differential diagnosis*. The more important and most frequent of these are *bronchiectasis*, *lung abscess*, *lung tumor*, *fusospirochetosis*, *pulmonary mycosis*, the *common pneumonias*, and *foreign bodies*.

**Bronchiectasis.**—The presence of bronchiectasis may be inferred from the history of longstanding and abundant *expectoration* without apparent *debilitation*. The physical findings on examination are often quite typical, but these as well as a suggestive history may be absent in the so-called “dry” phase. *Lipiodol bronchograms* are necessary to make a positive diagnosis. It is of course important to exclude tuberculosis as the cause of the bronchial dilatation through careful sputum examinations.

**Lung Abscess.**—As lung abscess may be confused with a tuberculous excavation by roentgen-ray, the *sputum examinations* are again of the highest importance. These are best done on the secretions aspirated from the affected bronchus by the

bronchoscopist. The clinical picture of a lung abscess due to nontuberculous bacteria is usually more pronounced in severity, although, as is well known, an acid-fast lesion is often complicated by pyogenic organisms.

*Fusospirochetosis.*—The independent work of David Smith<sup>1</sup> and Russell Haden<sup>2</sup> has done much toward our recognition of fusospirochetal lung disease in recent years. As *Vincent's organisms* are prone to invade the lower respiratory tree secondary to their oral involvement, this disease entity is frequently confused with basal tuberculosis. Through excellent animal experimentation, as well as human observations, Smith has shown the multiple pathologic processes which this anaerobic disease many assume. For early recognition, all sputum specimens should include routine studies for the *fusiform*, *spirochete*, and *vibrio* forms as well as for *acid-fast bacilli*. These are best found by searching in smears stained by gentian violet for the fusiform, and by silver nitrate (Fontana) for the spirochetes. When found, a second specimen should be examined in order to be certain that these organisms are from the lungs, after noting the following precautions:

1. The teeth are brushed several times.
2. The mouth is rinsed thoroughly with some kind of sterile mouth wash.
3. The sputum is coughed up immediately afterward and is collected in a clean container and then washed through five changes of sterile saline.

The presence of numerous organisms of the fusospirochetal group in material obtained at bronchoscopy does tend to assure one of the freedom of mouth contamination.

*Pulmonary Mycosis.*—With the help of the mycologist, the clinician has become much more on the alert for fungous diseases of the lungs. The relative increase in the frequency of the diagnosis of this entity is probably due to our better technic in its recognition. Pulmonary mycosis is pre-eminently a disease of the lower lung fields. Usually it is of very chronic nature and therefore becomes one of the most confusing of clinical pictures, as is basal tuberculosis. Fungi will usually

give clear sterile effusions. *Monilia albicans* infection will especially simulate tuberculosis, in causing cavities, hemoptyses, effusions, and spontaneous pneumothoraces.

The differential diagnosis here rests entirely upon careful examinations of the sputum, although a positive skin test to an extract of the offending fungus will be helpful. The sputum specimen is examined on smear or hanging drop preparations, cultures, and animal inoculations. The slide preparation for finding actinomyces is similar to the one for tubercle bacilli, *i. e.*, smearing the suspected material between two slides. In searching for cultures of fungi, the sputum specimen should be implanted on both Sabouraud's dextrose agar media (meat extract agar with 1 per cent dextrose, preferably with a pH of 4 to 5) and blood agar. The yeast-like fungi (*endomyces*, *saccharomyces*, *monilia*, *cryptococcus* (*Torula*), *blastomyces*, *Geotrichum*, *coccoidal granuloma*, *sporotrix*, and *histoplasma*), and mold-like fungi (*aspergillus*, *penicillium*, and *mucor*) will grow on the former, while the higher bacterial forms (as the *anaerobic*, *aerobic*, and *acid-fast actinomyces*) require the latter media for growth. When a pure culture of a suspected pathogen is found, this fungus should be tested for agglutination by the patient's serum as well as animal inoculation for reproduction of the disease. The intravenous route is preferable in the latter. (A tuberculin test should be done before autopsy when using guinea-pigs.)

*Lung Tumors.*—Lung tumors (particularly *bronchogenic carcinomas*) often give a bizzare clinical picture when occurring in the lower lung fields. These may be confused with tuberculosis on roentgen examination due to the picture of atelectasis, emphysema, and suppurative pneumonitis secondary to the obstructed air passages. Biopsy of the lesion on bronchoscopy, recovery of the tumor cells (in sputum or on bronchial aspiration), or a lung punch biopsy done under favorable conditions (when the lesion is near the pleural surface with an obliterated pleural sac) will verify this entity. The relatively *short duration of symptoms*, *presence of pain*, and *clinical picture of sepsis* (the latter due to the suppurative

pneumonitis) should lead one to suspect tumor in favor of tuberculosis. A bronchostenosis of tuberculous etiology may, of course, present this same symptomatology.

*Foreign Bodies.*—Foreign bodies in the lower air passages, if of long standing and not radiopaque, may present a clinical picture comparable to tuberculosis. The presence of a foreign body in a lower bronchus<sup>3</sup> may be suggested by a positive *history* of inhalation of substance along with the demonstration on physical examination and roentgen studies of the *obstructive emphysema*. The diagnosis is then confirmed by bronchoscopic removal.

*Nontuberculous Pneumonias.*—Uncomplicated nontuberculous pneumonias in the lower aspect of the lungs are, as a rule, less confused with true acid-fast disease than the above. The exceptions are the rarer forms, such as the *virus* and *Friedländer* types, which tend to have a longer course. The common pneumonias will usually be correctly recognized through the usual examinations, including *sputum smears* and *culture*, *specific typing*, *blood culture*, and the relatively *short clinical course*. It must be remembered that the diagnosis of unresolved pneumonia is made with hazard, this often proving to be tuberculosis.

*Diagnosis.*—The diagnosis of basal tuberculosis is made with surety only by finding the *bacilli in the sputum on gastric aspiration* and proving them to be *Koch's bacilli* through *guinea-pig inoculation*. As is illustrated in one of the following case reports, *multiple* sputum specimens may be necessary before a positive one is obtained. As the symptomatology, physical findings, and roentgen studies may simulate many other disease processes, the *actual demonstration* of the bacilli is the *only* complete assurance to the clinician. In the absence of this finding, tuberculosis may be inferred only after exclusion of the other many possibilities with our laboratory facilities.

It should be remembered that a positive tuberculin test is inconclusive help in establishing the diagnosis. On the other hand, a negative tuberculin test will exclude the disease except

in the primary form of the disease of less than ten days' existence and in the very ill patient.

**Illustrative Cases.**—The following two cases are illustrative of basal tuberculosis:

**Case I.**—A sixty-three-year-old man first came to the Clinic on December 29, 1938, with the major complaints of weakness and weight loss over a three-year period, and attacks of dyspnea of six weeks' duration. An analysis of his past history prior to the past three years revealed nothing of significance. There was a suggestive history of tuberculosis in a brother.

The patient dated the onset of his present illness from a "nervous breakdown" three years before, describing this as being an episode of exhaustion, weight loss (38 pounds), and nervousness. After resting ten weeks, he felt better and worked until September, 1938, although the symptom of lessened endurance was progressing. In September, 1938, he developed fever to 102° F. with delirium and was diagnosed as having pneumonia. After several weeks of persistent low fever, a chest roentgen-ray was taken and reported as "unresolved pneumonia." Soon after this, he began to have attacks of shortness of breath. These were characterized as a feeling of substernal fullness, progressing toward the throat, with associated expiratory wheezing. These attacks were more frequent nocturnally.

The patient was referred to the Clinic with the presumptive diagnoses of unresolved pneumonia or lung tumor. A recent guinea-pig inoculation had been reported as being negative. The review of systems revealed symptoms of glossitis of three years' duration and paresthesias of all extremities, with difficulty in walking for from six to eight weeks. There had been a weight loss of 65 pounds in the past three years.

The general physical examination revealed a chronically ill individual who evidenced much loss of weight. The skin was pale and dry. The tongue was red and atrophic. The chest expansion was lessened on the right side, with decreased per-

cussion note over the right side, from the seventh to tenth vertebral spine posteriorly and the fourth to sixth rib anteriorly. The breath sounds were diminished over the entire right back with numerous moderately coarse crepitant râles heard at the right base. Neurologic examination revealed an almost total loss of vibratory sensation in all extremities. The remainder of the general physical examination revealed entirely normal findings except for a temperature of 99.6° F.

Stereoroentgenograms of the chest (Fig. 60) revealed a nodular infiltration in both lower lung fields with a large opaque



Fig. 60.

Fig. 61.

Figs. 60, 61.—Progress films in Case I, showing progression of right basal lesion to upper lung parenchyma and left pleural effusion.

circumscribed area of 5 cm. diameter in the lower right lung. Roentgen studies of the gastro-intestinal tract revealed non-visualization of the gallbladder (with two doses of dye) and a small diverticulum in the left colon. A scout film of the abdomen showed a destructive process in the upper right border of the third lumbar vertebra.

In the laboratory studies, three sputum specimens were negative for acid-fast bacilli and fusospirochetes. On culture, *saccharomyces* developed from each specimen. The gastric analysis revealed an absence of free hydrochloric acid. Stool

examinations were negative. Special blood counts showed a macrocytic type of anemia with a volume index of 1.06.

Feeling that this patient's chest pathology might be due to pulmonary mycosis (saccharomycosis) it was decided to use potassium iodide, thymol, and autogenous vaccine (of the yeast culture). He was therefore given these medications along with the routine liver extract therapy (parenterally) for his pernicious anemia. He slowly but definitely showed clinical improvement, although a follow-up roentgenogram showed very little change in the pulmonary pathology.

In the succeeding eight months following his initial examination at the Clinic, the patient was seen at monthly intervals, with his active treatment being given by his family physician. At each visit to the Clinic, sputum specimens were examined for acid-fast bacilli and it was not until the eighth month that a few of these organisms were found and proved to be true Koch's bacilli through guinea-pig inoculation. At the last visit, a pleural effusion had developed (Fig. 61) with spread of parenchymal lesions.

**Case II.**—A twenty-nine-year-old stenographer was seen at the Clinic on February 8, 1938, with the chief complaint of attacks of pleurisy with cough over the previous six-year period. During this time it was established that she had had five definite pleural effusions, each effusion having been treated by removal of amounts varying between 200 cc. to 500 cc. of clear, straw-colored fluid. The patient had had roentgen examinations and sputum studies with each of the above attacks, all being negative for evidence of lung disease. A tuberculin test had been reported as negative five months prior to being seen at the Clinic. In the past four months she had had a constant productive cough, frequently raising blood-tinged sputum. The tentative diagnosis had been bronchiectasis.

The past history and review of symptoms were noncontributory. There was no family history of tuberculosis.

The general physical examination revealed a well developed, fairly well nourished individual. The only significant

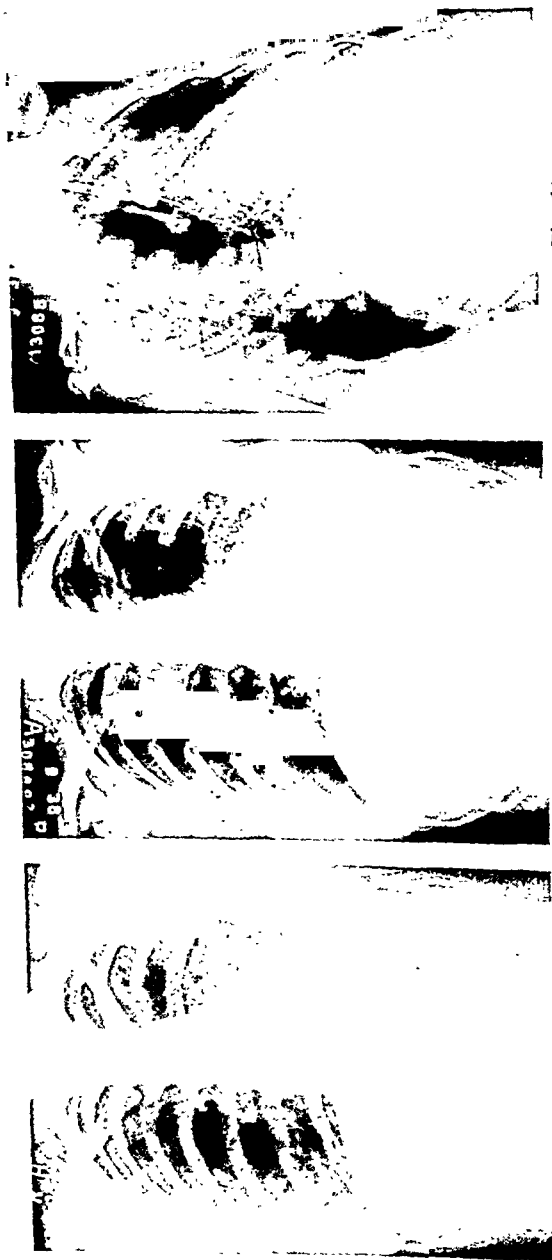


Fig. 64.

Fig. 63.

Fig. 62.

Figs. 62, 63, 64.—(Case II.) Left basal lesion with lipiodol bronchograms, revealing a minimal fusiform bronchiectasis of tuberculous etiology.

findings were confined to the chest. The expansion was lessened on the left side, with decreased note over the left base posteriorly from the sixth to the tenth vertebral spine. Numerous moderately coarse, crepitant râles were heard in this region, both anteriorly and posteriorly. The rest of the physical examination revealed entirely normal findings.

Stereoroentgenograms revealed a fibrous infiltration in the left lower lobe (Fig. 62) interpreted by the x-ray department as being compatible with bronchiectasis. Lipiodol bronchograms (Figs. 63, 64) showed a minimal degree of bronchial dilatation of fusiform type. A single sputum specimen revealed acid-fast bacilli. The erythrocyte sedimentation rate was moderately elevated.

The patient was advised to have sanatorium care. Subsequent reports revealed that the patient suffered a progression of the disease to the left upper lobe with a tuberculous bronchitis (on bronchoscopic examination). An eight rib thorocoplasty was performed in September, 1939, with good collapse and the sputum has remained negative to date.

**Summary.**—The basal chest lesions of tuberculosis have always been a confusing problem to the diagnostician. As in apical infection with this disease, the symptomatology, physical findings, and clinical course may simulate other lung diseases. Unlike tuberculosis of the upper lung fields, the roentgen studies of basal tuberculosis are not diagnostic. An accurate diagnosis can only be made by finding the true acid-fast bacilli by Koch's hypothesis.

Through our methods of recognition of the many other diseases affecting the lower lung fields gained in recent years, we are more capable of inferring tuberculosis by careful exclusion of nontuberculous diseases, even in the absence of the bacilli in sputum or gastric specimens. Our newer knowledge of pulmonary mycoses and fusospirochetal lung disease is particularly helpful.

The various clinical and laboratory aids in differential diagnosis have been stressed.

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## DUODENAL DRAINAGE: INDICATIONS AND TECHNIC

E. N. COLLINS

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ALTHOUGH we do not use duodenal drainage routinely in the investigation of the upper gastro-intestinal tract, in recent years it has been employed in an increasing number of cases and it has given information which could be obtained in no other way. Unusual diagnostic problems presented by patients whose gallbladders have been removed, whose jaundice is of a sufficient degree to contraindicate the use of cholecystography, or whose clinical and cholecystographic findings are indeterminate have proved the chief indication for the use of this procedure. In our experience, however, cholecystography has proved the most important single routine diagnostic procedure pertaining to the biliary tract.

The increasing interest in the study of the "*post-cholecystectomy syndrome*" has again emphasized the importance of earlier diagnoses in order to prevent the late sequelae of biliary disease. Allen O. Whipple,<sup>1</sup> in presenting a study of 700 unselected *consecutive* patients having biliary or pancreatic lesions operated upon by himself during the twenty-year period from 1914 to 1934, states, "The findings of cholesterol crystals, calcium bilirubin particles, and pus cells with bacteria in the duodenal contents obtained by duodenal intubation is, in our experience, even more reliable than cholecystography in demonstrating true pathology; that is, a lesion requiring surgical therapy." Medical management also is obviously most effective when instituted early in the course of biliary disease.

If we are to make an early diagnosis we believe the more widespread use of duodenal drainage, particularly in borderline cases, proves important. The indications for this procedure, according to our experience, are as follows:

## (A) IN DIAGNOSIS

1. *Suspected biliary disease; gallbladder has been removed*  
(post-cholecystectomy syndrome):
  - (a) Suspected common-duct stone.
  - (b) Chronic cholangitis.
  - (c) Stricture of common duct.
  - (d) Spasm of sphincter of Oddi; biliary dyssynergia.
2. *Suspected biliary disease; presence of jaundice:*  
History and physical findings indeterminate.  
No opaque stones visualized by roentgen examination.
3. *Suspected biliary disease; absence of jaundice:*
  - (a) History characteristic of biliary colic.  
Cholecystographic and other roentgen findings normal.
  - (b) History and physical findings indeterminate; other causes for patient's symptoms excluded.
    1. Normal cholecystographic findings, or
    2. Non-visualization of the gallbladder by cholecystography and no opaque stones visualized.
4. *Suspected pancreatic disease.*
5. *Certain diseases of the liver, such as biliary cirrhosis.*
6. *Postoperative appraisal of state of biliary tract.*

## (B) IN TREATMENT

Pancreatitis; "catarrhal" jaundice; biliary dyssynergia; non-calculous biliary tract disease; intractable urticaria; the use of a vaccine made from cultures of bile.

**Significant Abnormal Findings on Duodenal Drainage**

1. Absence of concentrated bile (gallbladder present):  
Repeated stimulations; possibly repeated on separate days.  
Correlations with roentgen findings:  
Consider abnormal function of gallbladder, cystic duct obstruction, or gallbladder containing stones; psychic factors.

## 2. Presence of:

(a) Cholesterol crystals.

(b) Calcium bilirubinate pigment.

1. *If jaundice is not present:* Presence of either (a) or (b) usually indicates gallstones, cholesterosis, or precalculous state. The presence of both (a) and (b) pathognomonic of biliary calculi.

2. *If jaundice is present less than a month* (or has been present recently): Presence of (b) alone is not significant. Presence of (a) alone may indicate cholesterosis. Presence of both, as indicated in (1). In an occasional patient who has been jaundiced longer than a month, the finding of either or both *may not indicate* the presence of stones.

**Suggestive Abnormal Findings on Duodenal Drainage**

1. Unusual number of bile-stained pus cells.
2. Abnormal cell exfoliation.
3. Bacterial clumps—number and amount in concentrated or last bile fractions.
4. Bacteriologic examinations.

**Technic of Duodenal Drainage.**—The value of duodenal drainage depends to a great extent on the *care* and *exactness* of the technic used, as well as the *experience* of the examiner. Although these criteria are always employed in judging the value of cholecystography and other laboratory procedures, they may not be given equal emphasis in the appraisal of duodenal drainage. This communication is based on the work done or supervised by a technician who has had ample training and experience with Doctors Lyon and Bockus. Because of its demonstrated value in producing contraction of the gallbladder during cholecystography, an egg-yolk-lecithin-glycerine mixture,<sup>2</sup> has been injected through the duodenal tube when no concentrated bile (gallbladder present) is obtained by the use of the usual stimulants.

The *details* relative to the technic of duodenal drainage have been published by Lyon,<sup>3, 4</sup> Rehfuss and Nelson,<sup>5</sup> and others.

*Positive* findings may be accepted with greater certainty than negative findings, as is the case with other laboratory procedures. When there is *absence of concentrated bile* (gallbladder present) and the result of duodenal drainage is either indeterminate or not in keeping with other features of the individual's problem, *recheck examinations* should no more be neglected in the appraisal of duodenal drainage than is the case with other examinations.

The value of experience in *interpretation* has been emphasized by Shay and Riegel<sup>6</sup>: "Persistence and care are required even by the very experienced microscopist. Examination of the sediment after centrifugalization should always be made before the specimen is to be considered negative and it is of great importance that the material be examined shortly after it is obtained."

In attempting to relax the sphincter of Oddi and promote drainage of bile, it should be recalled that the administration of magnesium sulfate and other gallbladder stimulants by mouth produces a result different from that obtained by introducing the substance directly into the duodenum. Not only is hypertonic magnesium sulfate reduced to isotonicity in the stomach, but at least a part of the solution is converted into magnesium chloride, and when it reaches the duodenum, the union with sodium results in its conversion to sodium sulfate. Physiologists have reported that sodium sulfate tends to constrict instead of relax involuntary muscles.

**Cholecystography.**—Our experience relative to the value of cholecystography has been published.<sup>7, 8</sup> Cholecystography and other roentgen examinations are done routinely on patients suspected of having biliary disease who have a gallbladder and who are not jaundiced.

In the interpretation of these findings we do not believe sufficient emphasis has been placed on the *limitations* of cholecystography. For example, normal cholecystographic findings

do not exclude the presence of a significant cholecystitis. We must recall the fact that a gallbladder full of calcium-type gallstones often functions normally, as determined by cholecystography and, in this instance, a diagnosis of chronic cholecystitis, as well as cholelithiasis, is usually made in spite of the normal function.

Of the relatively huge number of patients having cholecystography, only a small number have operations on the biliary tract. In our experience, few patients having normal cholecystographic findings have operations on the biliary tract, so that the accuracy of cholecystography as a diagnostic procedure in these instances is rarely checked at operation and by the pathologist. Those having non-visualization of the gallbladder by cholecystography without evidence of opaque calculi rarely have operations unless there is a history characteristic of biliary colic.

**Diagnosis.**—1. *Suspected Biliary Disease in Absence of Gallbladder.*—The value of duodenal drainage in cases of *common duct stone after cholecystectomy* has been demonstrated in the cases reported by Shay, Tumen, and Rodis,<sup>9</sup> and Shay and Riegel.<sup>6</sup> In these instances, roentgenograms of the gallbladder area may reveal an absence of opaque calculi and the findings obtained by duodenal drainage may give the clinician the most important objective evidence available. The presence of both cholesterol crystals and calcium bilirubinate is pathognomonic of common duct stone, regardless of the presence or absence of jaundice. If jaundice is present or has been present recently, the presence of calcium bilirubinate pigment alone is not significant, while the presence of cholesterol crystals alone may indicate the presence of cholesterol stones.

When *chronic cholangitis* is present, abnormal amounts of the products of inflammation are obtained by duodenal drainage, such as bile-stained pus cells, excessive cell exfoliation, bacterial clumps, and positive cultures on bacteriologic examination. The value of a positive culture in these instances has been open to question unless scrupulous technic is used, the same type of organism has been recovered on each of several

drainages, and the organism is not one likely to be due to contamination. If calculi are associated with the infectious process, the findings mentioned in the preceding paragraph may also be present.

The diagnosis of *stricture of the common duct* is often obvious from the history and physical findings. However, in any patient having jaundice, duodenal drainage is a significant procedure because it determines at once whether or not bile is reaching the intestinal tract and the relative amount (in conjunction with the *icterus index* curve). It also permits examination of the bile itself. One or more stones remaining in the common duct after surgery on the biliary tract may be the cause of the symptoms, or there may be a combination of stones and stricture.

On the other hand, the absence of significant findings by repeated duodenal drainage may result in the diagnosis of *biliary dyssynergia*. This procedure has also proved to be a valuable therapeutic measure in this condition when other methods of treatment have been ineffective.

2. *Suspected Biliary Disease; Presence of Jaundice.*—In simple problems where there is a history of biliary colic followed by jaundice, the diagnosis is apparent. This is especially true when roentgenograms of the gallbladder area reveal the presence of opaque calculi or when the jaundice has subsided; cholecystography demonstrates the presence of gallstones. But when the clinical and roentgen findings are indeterminate, duodenal drainages are helpful in differential diagnosis. While jaundice is present cholecystography is not used and plain films may show no opaque calculi.

Other diagnostic measures which have proved significant in our experience have been quoted by Phillips and Haden,<sup>10</sup> and Hartsock.<sup>11</sup> Repeated examinations of the *urine* and stools for bile pigment and a curve plotted from daily or repeated determinations of the *icterus index* are especially significant in following the course of the disease. Hartsock has mentioned that, "There are many cases in which the exact etiology of the jaundice remains in doubt even after explora-

tory operation, so it is easy to realize the difficulty of making an exact diagnosis clinically."

3. *Suspected Biliary Disease; Absence of Jaundice.*—In cases where jaundice is not present and the cholecystographic findings are normal, biliary disease may still be suspected. The patient may or may not give a history characteristic of biliary colic and other causes for the symptoms have been excluded. We believe the *assumption* that the biliary tract is *normal* because the cholecystographic findings are normal is *incorrect*.

Jenkinson<sup>12</sup> found that in a series of ninety-five cases with symptoms referable to the gallbladder, cholecystography showed a normally functioning gallbladder in seventy (73 per cent). Graham and Mackey<sup>13</sup> suggest that a proportion of unsatisfactory results in gallbladder surgery arise from mistaken diagnosis. The normal cholecystogram should not be a warning against operation. In dealing with operations on the stoneless gallbladder, Graham and Mackey found the same percentage of cures or improvement in the group of patients with normal cholecystograms as in the group with non-visualized gallbladders (60 per cent). In the same type of case Kunath<sup>14</sup> stated, "of the cases in which there were normal cholecystograms, there were cures or improvement in 75 per cent."

Therefore, *in spite of normal findings by cholecystography*, when a strong suspicion of biliary disease remains, we believe significant abnormality in the biliary tract should not be considered to have been excluded until *two or more duodenal drainages result in normal findings*. The chief purpose of this presentation is to emphasize *early* diagnosis in biliary tract disease. When other factors in an individual problem are indeterminate, positive findings by duodenal drainage may result in a diagnosis of cholesterosis, a precalculous state, or chronic cholangitis. If early surgical procedures do not seem to be indicated, the use of the important developments in medical management should prove especially valuable in these cases.

3. *Non-visualization of the Gallbladder by Cholecystography.*—Non-visualization of the gallbladder by cholecystography (no opaque calculi visualized) does not mean that the

cause for the patient's abdominal symptoms has been found. Unless there is a history of *unquestioned* biliary colic, it is advisable for the surgeon to defer operation on the biliary tract until *roentgen* and other examinations of adjacent organs, as well as *duodenal drainage*, have been done. Close correlation of all clinical and laboratory evidence is, of course, assumed in order to prevent an unsatisfactory postoperative course.

When the multiple dose technic is used in cholecystography, non-visualization of the gallbladder without evidence of opaque calculi often indicates a non-functioning gallbladder containing calculi of the cholesterol type, possibly blocking the cystic duct. But consideration must also be given to the possibility of other causes of non-visualization, such as disease of the liver or disease in adjacent organs which may cause reflex disturbance in the dye-concentrating ability of the gallbladder or dysfunction in the sphincter of Oddi. An active duodenal ulcer or hypothyroidism may result in non-visualization. In other words, *non-visualization does not necessarily indicate a pathologic gallbladder*, and such a diagnosis should not be made unless there is a suggestive history of biliary disease and roentgen examination of adjacent organs reveals no evidence of abnormality.

The findings on duodenal drainage may show that operation is clearly indicated. On the other hand, when satisfactory duodenal drainages result in normal findings and there is no clear-cut history of biliary colic, we believe considerations relative to surgery should be deferred. Recheck cholecystograms made after medical management may reveal normal findings.

Jenkinson<sup>12</sup> found that in eight, or 40 per cent, of twenty patients with non-functioning gallbladders by cholecystography there was a normal response radiographically after medical management.

We agree with Wilkinson<sup>13</sup> in his discussion of "Chronic Cholecystitis Versus Irritable Colon" when he states, "The fundamental difference between the diagnosis of chronic cholecys-

titis and that of irritable colon would be of little moment but for the fact that one condition is organic and likely to be treated surgically while the other is a functional disorder amenable to dietary management. Since there is such a similarity in the two types of complaints, it does not seem proper immediately to classify chronic dyspepsia as gallbladder disease because of a dull ache in the right upper part of the abdomen and a poorly seen gallbladder. Lahey and Jordan have shown that 44 per cent of the patients with chronic dyspepsia whose gallbladder cannot be visualized will later show normal filling after an adequate period of bowel management. The patients who show delayed emptying or poor visualization will be even more likely to fall into the functional group."

This coincides with our experience except that a smaller percentage of our patients having irritable colon have a non-functioning gallbladder by cholecystography at the initial examination with return to normal function later. Differences in cholecystographic technic used at the time the statistics were compiled may be the explanation.

The significant feature is the established fact that *spastic conditions* of the gastro-intestinal tract *can cause temporary non-visualization* of the gallbladder by cholecystography. In this group most of our patients did not have duodenal drainages at the time of the original examination because the symptoms relating to the irritable colon syndrome, associated with diarrhea or constipation, or one alternating with the other, seemed most significant. If recheck cholecystography at the end of a period of adequate bowel management does not result in normal findings, we now routinely request duodenal drainage.

In our experience, one of the chief causes of the *increasing incidence of irritable colon* is the widespread use of magnesium sulfate given by mouth each morning for months if not years as a supposed "cure" of alleged gallbladder disease. We refer to patients who do not give a history of clear-cut biliary colic but have non-visualization of the gallbladder by cholecystography associated with an indeterminate chronic dyspepsia. Even though the symptoms involve the right upper abdominal

quadrant (usually close analysis of symptoms will reveal the presence of abdominal distress related to other parts of the colon also) we have found that the discontinuance of the increasing use of cathartics, particularly daily saline cathartics, together with other principles of bowel management, result not only in relief of symptoms but a return to normal in gall-bladder function.

The difference in giving hypertonic *magnesium sulfate* by *mouth* and by *duodenal tube* (after which it is immediately removed by siphonage during duodenal drainage) has been emphasized earlier in this discussion.

4. *Suspected Pancreatic Disease*.—When suspected pancreatic disease is present, the analysis of the findings on duodenal drainage is of unquestioned value. On the diagnostic side, it is important when *purulent material* or other *inflammatory products* are obtained, as well as to permit analysis of the character of the duodenal contents, including studies of *pancreatic enzymes*. Constant duodenal drainage while adequate parental therapy is administered has also proved important from the therapeutic standpoint.

5. *Certain Diseases of the Liver*.—In the appraisal of certain diseases of the liver, such as *biliary cirrhosis*, we have found use of duodenal drainage important.

6. *Postoperative Appraisal of Biliary Tract*.—In the postoperative evaluation of the state of the biliary tract, we believe the findings obtained by duodenal drainage have not been sufficiently utilized, in view of the fact that it is desirable to prevent the "post-cholecystectomy syndrome." The writings of Best and Hicken<sup>16</sup> relative to cholangiographic demonstration of *biliary dyssynergia* are of unusual significance in this respect. Even though meticulous operative procedures have been done, detritus may remain in the common bile duct which is not drained by the T-tube. Substances injected directly into the duodenum, in proper concentration, have proved more effective than the administration of the same substances by mouth, not only in producing relaxation of the sphincter of Oddi, but also in permitting analysis of drainage from the common bile duct.

If duodenal drainage has not been done prior to two months following operative procedures on the biliary tract, we believe the more common use of this procedure at this time, in patients whose clinical course is not satisfactory, together with appropriate use of medical management according to the findings, will result in better operative statistics and the ultimate aim of a satisfied patient. It is fair to assume that the desirable postoperative course in the individual case, particularly when unusual circumstances are present, will be afforded by the mutual interest and cooperation of both the internist primarily interested in gastro-intestinal diseases and of the surgeon.

**Treatment.**—Our experience in the treatment of biliary disease by the use of duodenal drainage is limited. Our chief interest in this procedure has been its aid in diagnosis. We believe it is of value in the treatment of *pancreatitis*, in shortening the course of "*catarrhal jaundice*," in the treatment of the *postcholecystectomy syndrome*, and in *non-calculous biliary tract disease* when other well-known methods of medical management prove unsatisfactory. The use of a *vaccine* made from cultures of bile obtained by duodenal drainage has proved effective in the treatment of *intractable urticaria* when other procedures, from the standpoints of allergy and gastro-intestinal function, are ineffective.

**Conclusions.**—1. The increasing use of duodenal drainage in recent years, in correlation with cholecystography as well as with the clinical and other findings, has proved to be an important diagnostic procedure under the circumstances mentioned.

2. The most important indications for duodenal drainage are the instances where the gallbladder has been removed, where jaundice of a sufficient degree to contraindicate the use of cholecystography exists, and when both clinical and cholecystographic findings are inconclusive.

3. In patients having operations subsequent to duodenal drainage, the operative findings confirmed the findings by duodenal drainage in 84 per cent of all cases to date.

4. Since routine autopsies in various countries have shown

that half of the persons above the age of thirty years had pathologic changes in the gallbladder and approximately 20 per cent had gallstones, the more common use of duodenal drainage should result in earlier diagnoses and earlier operations, if medical management is not appropriate, before pathologic processes have extended so widely that surgery cannot be expected to relieve the patient's symptoms.

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## PERIPHERAL VASCULAR DISTURBANCES IN POLYCYTHEMIA

WALTER J. ZEITER

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POLYCYTHEMIA is a disease in which there is an increase in the number of red cells above normal. There is no absolute dividing line, however, between the normal and an abnormal number of red cells in the blood stream. Few men have 5,500,000 red blood cells per cu. mm. of blood, and any count above 6,000,000 per cu. mm. is usually abnormal. The comparable figures for women are 5,000,000 and 5,500,000 cells per cu. mm.

**Classification.**—This disease is divided into two major types, namely, *symptomatic polycythemia* and *polycythemia vera*.

Haden<sup>1</sup> classifies polycythemia as follows:

- I. *Symptomatic polycythemia*—increase in red cells without increase in blood volume (erythrocytosis), or increased blood volume without increase in red cell mass due to primary overproduction of erythrocytes to compensate for:
  - (A) Low barometric pressure
  - (B) Impaired oxygenation in lungs due to:
    1. By-passing of lungs by heart disease
    2. Decreased aerating surface in lung disease
    3. Decreased blood flow
  - (C) Impaired capacity of blood to carry hemoglobin, as in carbon monoxide poisoning
- II. *Polycythemia vera*—increase in erythrocytes with increase in blood volume and in red cell mass per kg. of body weight

(A) Symptomatic, from interference with oxygenation by:

1. Congenital heart disease
2. Ayerza's disease
3. Alteration of hemoglobin (as methemoglobinemia).

(B) Idiopathic, from unknown cause

**Etiology.**—The function of the red cell is to contain hemoglobin, the carrier of oxygen. If a condition occurs which interferes with the hemoglobin taking up its normal amount of oxygen, a simple compensatory increase in the number of red cells per cu. mm. may occur. This type of increase is known as *symptomatic polycythemia* or *erythrocytosis*. Here there is an increase in red cells without an increase in blood volume, or increased blood volume without increase in red cell mass due to primary overproduction of erythrocytes.

It is definitely known that people living at *high altitudes* often show symptomatic polycythemia. This is a reaction of the bone marrow to compensate for the diminished oxygen tension or lowered barometric pressure. This condition may be precipitated acutely in mountain climbers and aviators when at high altitudes. In *congenital heart disease*, in which part of the blood is not circulated through the lungs, improper or insufficient oxygenation occurs with resultant increase of red cells to compensate this deficiency. Another mechanism producing this increased number of red cells is a decreased aerating surface in the *lungs*, such as in *chronic fibrosing disease*. *Ayerza's syndrome*, in which the underlying pathology is pulmonary arteriosclerosis, or if syphilitic an obliterative endarteritis with periarteritis of the smaller intrapulmonary branches and arterioles, produces obstruction to bring about an increased red count. Marked *impeded blood flow*, as in extreme passive congestion of the portal system without cardiac or pulmonary disease, may produce symptomatic polycythemia. This picture can be produced also by *chemical poisons* which impair the capacity of the red cell to contain hemoglobin. This is noted

in carbon monoxide poisoning and occasionally in poisoning by coal tar derivatives, such as acetanilid, which causes methemoglobinemia.

In *polycythemia vera*, there is an increase in erythrocytes, with an increase in blood volume and in red cell mass per kg. of body weight. The etiology of idiopathic polycythemia vera is unknown.

**Diagnosis.**—Haden<sup>2</sup> is of the opinion that this condition cannot be diagnosed on an increased number of cells per cu. mm. alone, but that a definite increase in *blood volume* should be shown, which is always present in this disease.

The increase in red cells with *congenital heart disease*, *Ayerza's disease*, or a *toxic manifestation* producing polycythemia in which the blood volume and cell mass per kg. of body weight is increased, can be classified as a true polycythemia vera of symptomatic origin.

In *symptomatic polycythemia* or *erythrocytosis*, the red cell mass per kg. is not increased even with a high red cell count per cu. mm. or a high total blood volume per kg. of body weight.

The symptoms of polycythemia may be present and then disappear entirely. *Headache* and *vertigo* are very frequent complaints. *Weakness* of an arm or leg, *tingling* in hands and feet, *nervousness* and many other neurologic symptoms may appear. These are probably due to a disturbance in circulation brought about by the increased blood volume and the high blood viscosity which slows the blood flow. The slowed circulation also produces the *cyanosis* so frequently present in these patients. *Congestion of the vessels of the conjunctiva*, *redness of the palate* and *pharyngeal mucosa*, *enlarged spleen*, and occasionally *enlargement of the liver*, are common physical findings.

The *blood picture* shows an increase in the number of red blood cells, which may ordinarily range anywhere from 6,000,000 to 10,000,000 per cu. mm. The increase in blood volume and cell mass per kg. of body weight occurs as stated above.

Occasionally, *hypertension* of a more or less marked degree may be observed, in which case the symptom complex has been called *Geisböck's disease* or *polycythemia hypertonica*. This usually occurs in the patient past middle life with a certain amount of arteriosclerosis and probably should not be considered a separate entity from polycythemia vera.

The *clinical course* may run over many years. Frequently the patient has symptoms that are very *vague*, such as occasional dizziness, tinnitus, feeling of fullness in neck and head, discoloration of a toe which lasts for a short time and then disappears sometimes for a year or more. Since many of the patients are past middle life and have arteriosclerosis, *vascular complications* are frequent. Lesions are not uncommon in the cerebral, coronary, intra-abdominal (such as the splenic, hepatic, portal), and peripheral vessels.

In a review of thirty-one cases of polycythemia vera seen at the Cleveland Clinic in the past eight years, vascular disturbances occurred in nine patients, or approximately 29 per cent. Of these nine patients, six had peripheral vascular lesions. These all occurred in idiopathic polycythemia vera (see table, p. 489).

Four of the patients with peripheral vascular lesions ranged from sixty-two to seventy-five years of age, and three of the four had definite hypertension.

**Illustrative Cases.**—The following case history presents the typical findings in a patient with *idiopathic polycythemia vera*:

*Case I.*—A white man, aged sixty-nine, was admitted to the Clinic on June 2, 1937. About one year prior to admission the patient had edema and soreness in the right small toe which lasted about three weeks and then disappeared. Six weeks before admission the patient developed pain and discoloration in the great toe of the right foot and also in the left great toe, which was not as severe as the right. Three days before admission the entire right foot became edematous and the skin very red and bluish in color.

Case No.	Sex, age.	Symptoms of vascular disease of legs.	Diagnosis.	Red cells, in millions per cu. mm.	Hematocrit reading, cc. per 100 cc.	Mean volume of blood in cc. per kg. b. w.	Mean red cell mass in cc. per kg. body weight.
Normal. . . . .							
I	M. 69	Ulceration of both great toes.	Male Female	4.5-5.0 4.0-4.5	45 40	65 65	30 27
II	M. 70	Small ulcer on left heel. Intermittent claudication left calf. Right leg amputated because of gangrene of toes.	Arteriosclerosis obliterans with occlusion in both legs of posterior tibial and dorsalis pedis arteries. Varicosities.	8.33	73	121	89
III	M. 62	Cyanosis and pain 3-4 toes of right foot.	Arteriosclerosis obliterans and occlusion of left popliteal, posterior tibial and dorsalis pedis arteries.	6.90	64	92	59
IV	M. 43	Pain and edema right foot. Pain and edema of middle toe of left foot.	Arteriosclerosis obliterans, occlusion of left dorsal is pedis artery. Right artery pulse very weak. Varicose veins.	9.20	72	135	97
V	M. 64	Cyanosis and pain left great toe and small toe.	Chronic arterial disease.	7.10	63	90	57
				6.21	55	71	38

## ERYTHROMELALGIA IN A PATIENT WITH POLYCYTHEMIA VERA

Case No.	Sex, age.	Attacks of burning in toes with increased warmth.	Erythromelalgia in a patient with polycythemia vera.	Red cells, in millions per cu. mm.	Hematocrit reading, cc. per 100 cc.	Mean volume of blood in cc. per kg. b. w.	Mean red cell mass in cc. per kg. body weight.
VI	F. 55			4.77	43	87	38

Examination revealed a blood pressure of 170/110; the heart was not enlarged. The pharynx was intensely red. The right great toe was bluish-gray, which discoloration extended to the inner side of the foot; the dorsum was very red. The left great toe showed impaired circulation and some infection around the nail. Both toes were cold. The dorsalis pedis and posterior tibial pulsations were absent in both extremities. The radial arteries were thickened. A study of the blood showed 8,330,000 red blood cells; the hematocrit reading was 73 cc. per 100 cc. of whole blood. The blood volume was 121 cc. and the red cell mass 89 cc. per kg. body weight. The urine showed 3+ albumin, which disappeared to a trace at the end of a week in the hospital. The urea concentration in the blood was slightly elevated. The blood Wassermann and Kahn reactions were negative. The diagnosis was polycythemia vera and arteriosclerosis obliterans. On June 16, 1937, the right toe was amputated.

The blood studies showed that the number of red cells was 8,330,000, the packed cells definitely increased, the volume of blood per kg. of body weight was nearly doubled, and the red cell mass per kg. body weight was three times the normal amount. From these figures one can see the tremendous increase in total blood volume and red cell mass. From this picture it is not difficult to visualize why peripheral vascular lesions occur, especially when an arteriosclerotic process is superimposed.

The following is the history of *Case V in the tabulation*:

*Case II.*—A white man, aged sixty-four, was admitted to the Clinic on October 3, 1939. About four months prior to admission the patient did some excessive walking and developed pain in his feet. His toes became red, painful and slightly discolored at the tips. Various treatments were tried, such as heat, arch supports, and suction pressure treatment.

Examination of the patient revealed a blood pressure of 180/110. There was no enlargement of the heart. There was slight congestion of the conjunctivae and the ears were

quite red. The spleen was not palpable. On examination the feet were found to be quite warm, the toes were red, and discoloration was present over the distal end of the left great toe and over the left small toe. The dorsalis pedis and posterior tibial vessels revealed a good pulse. Oscillometric readings above the left ankle revealed an oscillation of  $4\frac{1}{2}$  and the right leg was 5. Roentgen examination of the left foot showed some calcification of the digital arteries. The blood study revealed 6,210,000 red blood cells; the hematocrit reading was 55 cc. per 100 cc. of whole blood. The blood volume was 71 cc. and the red cell mass 38 cc. per kg. of body weight. The urinalysis was normal and the blood Wassermann and Kahn tests negative.

In this case it will be noted that the blood findings are not markedly increased, but they are sufficiently so to be classified as a true polycythemia vera. In spite of the fact that the pulse in the dorsalis pedis and posterior tibial arteries was good, the increased blood volume and cell mass with a mild arteriosclerotic disease of the digital arteries produced circulatory disturbances.

**Treatment.**—The treatment of *symptomatic* polycythemia should be to remove the underlying cause, if such is possible. In *idiopathic* polycythemia vera, the treatment is directed towards the prominent symptom and not at the actual cause since this is unknown.

Treatment is based on destruction of the excess of red blood cells by some *hemolytic poison*, depressing red cell formation by *irradiation* or *arsenic*, or by removing excess blood by *venesection*.

*Acetyl phenylhydrazine* is an effective drug causing hemolysis of the red blood cells. The *dose* of the drug depends on the red cell mass to be destroyed. Usually a 0.1 gm. ( $1\frac{1}{2}$  gr.) capsule is given three times daily for from ten to thirty days. The drug action continues seven to ten days after it is discontinued, so it is important to follow the red cell mass closely or a marked anemia may result. When the red cell count is down to 5,500,000, it is wise to *discontinue the drug*. While the medi-

cation is taken, a mild jaundice may occur and also produce a dark urine due to the destruction of the red cells.

*Roentgen* or *radiation therapy* is used to depress red cell formation. The red cells are usually formed in the flat and short bones; however, in polycythemia vera, the normal yellow marrow changes to red in the long bones which produce red blood cells. Therefore, the exposures must be used over the long bones as well.

Therapy to the *spleen* does not depress the formation of red cells because it only acts as a reservoir for the increased number of red cells.

Arsenic will depress red cell formation just as it does white cell formation in leukemia.

A safe method for treating the patient with *polycythemia vera* is by *periodic bloodletting*. After a complete blood study, the red cell mass is definitely known, and since the normal red cell mass is established, it is possible to calculate the approximate amount of blood to be removed. After the determined amount of blood has been removed, the blood volume and red cell mass may still be above normal. This is due to the excess number of cells stored in the marrow and in the spleen which are released into the circulation. It is not necessary to repeat the complete blood study after each phlebotomy; the *hematocrit reading* gives a fairly accurate index of the decrease of blood. By this method it is possible to watch the blood closely without producing a marked anemia. An attempt is made to keep the patient's red cell mass slightly below normal.

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## THE RÔLE OF GASTROSCOPY IN THE DIAGNOSIS OF GASTRIC DISEASES, WITH ESPECIAL REFERENCE TO PEPTIC ULCER AND CARCINOMA

J. F. RENSHAW

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It is well known that gastroscopy is a valuable adjunct to other methods of diagnosis of gastric disease. However, it is frequently asked, "Which patient should have a gastroscopic examination?" We believe that the following set of conditions are established *indications for gastroscopy* and we consider a gastroscopic consultation necessary when:

1. The gastro-intestinal roentgen findings are negative but one still suspects a gastro-intestinal disease.
2. The roentgen findings are inconclusive, inconsistent, or inadequate.
3. A gastric ulcer has been demonstrated radiologically.
4. A gastric carcinoma has been demonstrated radiologically.
5. A patient has had a gastric operation.

### NEGATIVE ROENTGEN FINDINGS

It is impossible to say which of these groups of conditions is the most important one. Certainly, the demonstration of a marginal ulcer is important to the patient with a gastro-enterostomy and, likewise, the demonstration of an early ulcerating carcinoma is important to that patient. However, the largest number of patients who should have a gastroscopic examination are in the first group, namely, those with negative roentgen findings where one still suspects gastro-intestinal disease. It has been estimated by various authors that such patients constitute from 15 to 45 *per cent* of a general medical practice.

This group is important because the commonest disorders of the stomach cannot, for practical purposes, be demonstrated by any other clinical method except gastroscopy. We believe that chronic gastritis is one of the commonest, if not the most common, disease of the stomach. In the past year, 246 patients have had gastroscopic examinations at the Cleveland Clinic. Of this group, 135 patients, or 50.8 per cent, had some form of chronic gastritis.

**Case I.**—A twenty-three-year-old laborer, whose *chief complaint* was "stomach trouble." (Fig. 65, *A* and *B*.)

*Present illness:* For six years this patient had had dull, localized epigastric pain coming on one to two hours after eating. There was no seasonal variation, but it did seem to come in attacks with long intervals of freedom from distress between attacks. At first the pain was relieved by the intake of alkalies or food. In the past two years, however, the distress had become more severe and constant, and was not affected by food intake, alkalies, or bowel movements. Bowel habits had always been regular and there was no laxative habit.

The *physical examination* was essentially negative except that the patient was of the hyperkinetic nervous type.

*Laboratory examinations* revealed normal blood counts, urine specimens and blood Wassermann and Kahn reactions. A two-hour fractional gastric analysis, using 35 gm. of bread and 350 cc. of water for the test meal, revealed a free acidity varying from 30 to 70 units and a total acidity of from 40 to 100 units, with the highest acidity being at the end of the test. Duodenal drainage revealed the presence of increased number of bile-stained pus cells.

By *roentgen examination* the stomach and duodenum and gallbladder were normal and the sigmoid portion of the colon was spastic but free of organic disease.

In the *gastroscopic examination*, all parts of the stomach usually seen were well visualized. The gastroscopic diagnosis was hypertrophic gastritis, and the final clinical diagnosis was hypertrophic gastritis, cholangitis (?), and irritable colon.

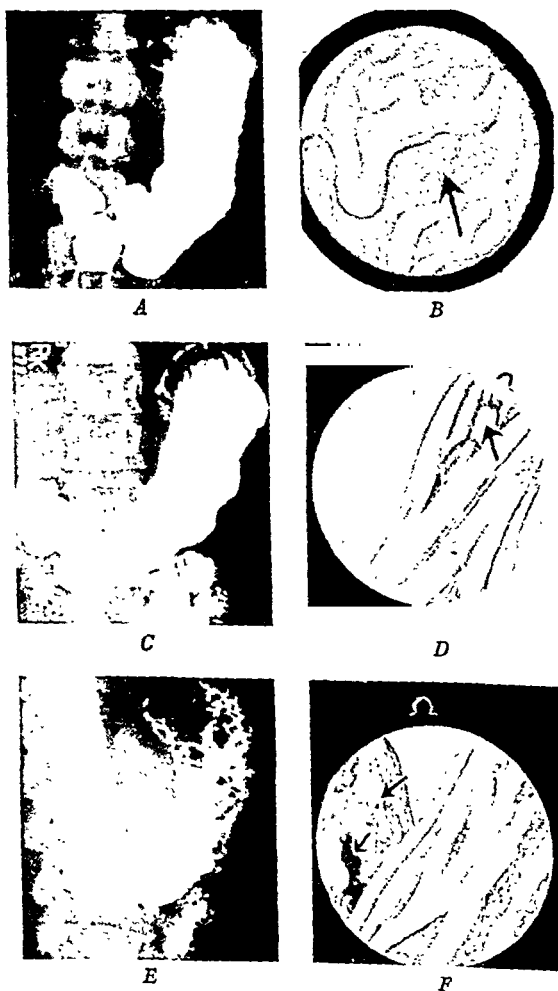


Fig. 65.—Negative roentgen findings (*A*, *C*, *E*) contrasted with positive gastroscopic findings; *B*, hypertrophic gastritis characterized by nodular changes between normal folds (see Case I); *D*, gastric ulcer with four small folds radiating from crater (see Case II); *F*, hemorrhagic hypertrophic gastritis with irregular dark area indicating one of the hemorrhagic areas (see Case III).

If the gastroscopic examination had not been made in the above case the true cause of the patient's distress would not have been discovered. All too frequently such cases are diag-

nosed "hyperacidity," "ulcer syndrome without ulcer," "gastric neurosis," or some other equally meaningless term. On the other hand, one must not assume that because the roentgenologist failed to demonstrate a lesion and because about one-half of all patients with hypertrophic gastritis have an ulcer-like syndrome that their distress is due to gastritis. Occasionally, a true gastric ulcer may be present, as in the following case. This patient had had a roentgen examination just before coming to the Clinic and one at the Clinic. Both examinations were reported as negative.

**Case II.**—A thirty-one-year-old office worker, whose *chief complaint* was "pain in the stomach." (Fig. 65, C and D.)

*Present Illness.*—This patient complained of pain in the stomach of twenty-one months' duration. It was localized in the epigastrium and in the right lower quadrant. Because of the latter pain, he had been operated on for chronic appendicitis without improvement. The epigastric distress was described as a soreness and burning. It had a definite relation to meals and it awakened him three times nightly. Because of dietary limitations, he had lost 30 pounds during twenty-one months. Five months before we saw him, he developed an agonizing substernal pain and subsequently he had electrocardiographic evidence of coronary thrombosis.

*Physical examination* revealed an asthenic, malnourished young man. The systolic blood pressure was 116 mm. of mercury and the diastolic pressure 78 mm. of mercury. Other than the slight diffuse abdominal tenderness, there were no abnormal physical findings.

The blood counts, Wassermann and Kahn reactions, stool examinations and sedimentation rate were normal. Two stool specimens were negative for ova and parasites. An Ewald test meal revealed 20 units of free hydrochloric acid and 60 units of total acid. The basal metabolic rate was minus 14 per cent. A radiogram of the chest was normal. With oral cholecystographic dye, the gallbladder functioned well, and there was no evidence of calculi. The stomach and duodenum

were normal. The electrocardiogram at this time was highly suggestive of coronary thrombosis.

A *gastroscopic examination* was considered and, after reviewing the electrocardiogram and other evidence, it was decided that no undue risk would be incurred. In the greater curvature there were two erosions, one estimated to measure about 5 or 7 mm. in diameter, the other one 2 mm. in width and 5 mm. long. In the midportion of the posterior wall of the body at the junction of the lesser curvature and posterior wall, there was a definite ulcer (easily seen by a group of observers, including the referring physician) which was typical of a benign lesion. The final diagnosis was benign gastric ulcer, erosive hypertrophic gastritis and coronary thrombosis.

Although most of the patients with negative roentgen findings and persistent abdominal distress will have chronic gastritis or other organic stomach disease, there are a large number who will have a normal stomach both by radiogram and by gastroscopy. It is usually said that about 20 per cent of all gastroscopic examinations reveal a normal mucosa. In our series, 30.4 per cent were found to be normal. We believe that our figure is 5 to 10 per cent higher than that given by other authors due to a difference in circumstances and to the type of patients examined.

For example, a patient with a "typical" history of irritable colon and none of the usual peptic ulcer syndrome ordinarily would not have a gastroscopic examination. In fact, many of these patients for one reason or another might have only a limited examination, such as a "colon survey," including only stool examination for parasites, Ewald test meal, proctoscopic and roentgen examination of the colon. Obviously, from such a survey we learn nothing about the stomach except the acidity. Recently we have included a gastroscopic examination in the survey because it can be done the same day as the other examinations and because we learn something about the condition of the stomach. However, we believe that every patient should have a complete examination if possible. Even when a com-

plete gastro-intestinal series is done, a certain number of patients should also have a gastroscopic examination. Many of these patients will have normal stomachs, and hence our figure of 30 per cent. However, on the other hand, chronic gastritis is fairly commonly associated with an irritable colon and the frequent finding of gastritis warrants gastroscopic examinations as shown in the following case.

**Case III.**—A forty-seven-year-old laborer whose *chief complaint* was "stomach trouble" of one year's duration (Fig. 65, E and F).

*Present Illness.*—Although the patient had been constipated for twelve years and had resorted to the use of laxatives frequently, he had not had indigestion nor abdominal discomfort prior to two years before coming to the Clinic. At that time he had what had been diagnosed as influenza because of the high fever and weakness. With this attack of influenza he passed what he described as tarry stools. Following his recovery from this acute episode he was subject to gas and belching spells. He then developed a burning epigastric distress coming on one and a half to two hours after eating. At times the distress would be partly relieved by the taking of food and at other times partly relieved by bowel movements. At no time, however, did these measures completely relieve him of distress.

*Physical examination* was essentially negative. The *laboratory examinations* revealed a normal blood, negative urine, negative Wassermann and Kahn reactions. Using an Ewald test meal and fractional extraction for a two-hour period, there was no free hydrochloric acid and the highest total acidity reached 40. At the end of one hour, histamine was given and, following the histamine, there was still a complete achlorhydria. Biliary drainage done on two occasions revealed findings suggestive of an inflammatory reaction. Pancreatic ferments were normal.

The *gastro-intestinal radiograms* revealed a normal gallbladder, stomach, duodenum and colon.

A *gastroscopic examination* revealed a typical hypertrophic gastritis. The final clinical diagnosis was hypertrophic gastritis.

Subsequent gastroscopic examination two months later revealed essentially the same findings and the patient's distress continued in spite of the fact that dietary and medical measures had relieved his constipation.

It would seem that this patient's distress, if not entirely due to the gastritis, was at least in a large part due to it. The failure of the dietary and medical management to relieve his symptoms, even though constipation had been corrected, would have been unexplained if a gastroscopic examination had been omitted. Many patients in this predicament are considered neurotic and some physicians lose interest in such a case. However, knowing that this patient had gastritis, other forms of therapy could be tried and the management extended over a longer period until he did obtain relief.

**Comment.**—The more common *symptoms* which make one think of gastric disease include upper abdominal pain, heavy sensations, pressure sensations, feeling of fullness, feeling of a lump in the abdomen, gas, belching, sour eructations, soreness, burning, nausea, vomiting, anorexia, loss of weight, or low-grade fever. There is, however, one other symptom which is an important indication for gastroscopy: namely, *chronic blood loss* from the gastro-intestinal tract. In the case of any unexplained anemia, the patient should have a gastroscopic examination. The frequency of erosions and small submucosal hemorrhages in gastritis is recognized, but it is not so well appreciated that these erosions and submucosal hemorrhages may be the source of chronic blood loss. Acute massive gastric hemorrhage is usually considered to be an indication for gastroscopy. Some foreign writers have said that as much as 10 per cent of all massive gastric hemorrhages is due to gastritis; however, none of the authors in this country have reported such a high incidence. In a total of 789 gastroscopic examinations done here at the Clinic and elsewhere, I have seen only two cases of massive hemorrhage definitely due to gastritis.

In the Clinic series of 246 gastroscopic examinations, there were no cases of hemorrhage definitely due to a gastritis. If the blood loss has been sudden and acute, and if gastroscopic examination is considered, it should be done seven to ten days after the pulse, blood pressure, and blood counts indicate that active bleeding has ceased. Some gastroscopists do it as early as four days. If the examination is delayed a month or so, as is the common practice, all evidence of the gastritis or erosion may have disappeared by that time.

#### INADEQUATE OR INCONSISTENT ROENTGEN FINDINGS

The second large group of cases in which a gastroscopic examination is indicated are those with inconsistent, inconclusive, or incomplete roentgen findings.

In this second group we consider those patients with bizarre filling defects or unusual changes. Antral defects and complete or partial pyloric obstruction are very important indications. We also consider the possibility of benign gastric tumors or polyps in this classification, as well as the possibility of extragastric tumors. Gastric syphilis and lymphogranulomatous diseases would also be classified here. And finally, we include those patients who have ulcer-like symptoms but in whom the roentgenologist is not able to demonstrate an ulcer crater, even though he does demonstrate a deformed duodenal bulb which is highly suggestive of duodenal ulcer.

**Case IV.**—A forty-nine-year-old attorney, whose *chief complaint* was "pain in the stomach" (Fig. 66).

*Present Illness.*—This patient had three distinct types of distress: The first one dated back five years previously when he developed a dull pain in the upper quadrants of the abdomen. This was associated with constipation, flatulence and belching and the symptoms were relieved by the passage of flatus or by a bowel movement. One year following the onset of this trouble, he was seized with an agonizing retrosternal pain, radiating to the left arm. This was diagnosed as a coronary thrombosis and he had noted several mild attacks on exertion in the four years following the first attack. Three years

after the onset of the present illness, or two years before being seen at the Clinic, he developed typical ulcer-like distress, characterized as a gnawing, burning pain localized in the epigastrium coming on two to four hours after eating, and invariably relieved by food intake or the use of alkalies. It was

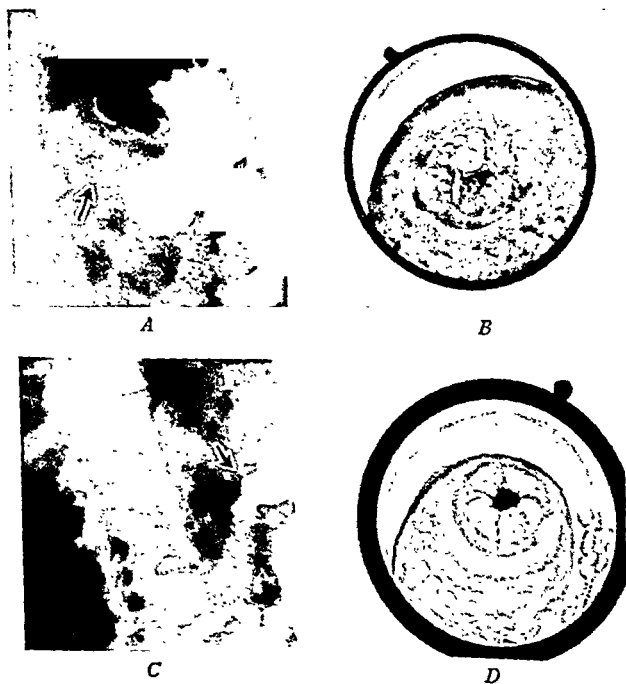


Fig. 66.—*A*, Antral deformity simulating carcinoma; *B*, mixed types of inflammation of the antrum, duodenal contents regurgitating through pylorus; *C*, antral deformity persisting three weeks after institution of treatment; *D*, typical hypertrophic gastritis, pylorus well visualized in contracted phase (see Case IV).

seasonal in occurrence and at times he would have nocturnal pain wakening him at two or three in the morning.

*Physical examination* revealed him to be obese. The heart was of normal size, but the electrocardiogram revealed a partial heart block, intraventricular block, and myocardial damage. The abdominal examination was negative.

The usual *laboratory examinations* were essentially normal. With the Ewald test meal the free hydrochloric acid was 30 units and the total acid 52 units.

The *roentgen examination* revealed a normal gallbladder. In the distal prepyloric portion of the stomach there was a filling defect through which peristalsis was not observed to pass. The duodenum was normal; the colon was normal except for a marked diverticulosis. Radiogram of the chest was normal. It was the roentgenologist's impression that the gastric filling defect was probably neoplastic, but progress studies were indicated.

A *gastroscopic examination* was easy in spite of the patient's obese, pyknic build and the cardiac difficulty. All parts of the stomach were well seen, including the lesser curvature of the antrum. Peristalsis was observed to pass through the antrum, and the pylorus closed completely with some regurgitation of duodenal contents. The diagnosis at that time could not be made with certainty; however, the process was thought to be inflammatory rather than neoplastic and it was requested that progress studies be done.

After a month of modified ulcer management with alkalies, antispasmodics and sedatives both gastroscopic and roentgen examinations were repeated. The defect radiologically appeared to be about the same as on the previous examination, although peristalsis did pass through it. The radiologist considered that the process might be inflammatory, but the diagnosis was not definite. However, on gastroscopic examination, the visualization was much more satisfactory than the first time. This time there were definite hypertrophic changes in the antrum, consisting of a lack of luster, a velvety mucosa, and granular nodular changes. Again peristalsis was observed to pass through this area. At this time the gastroscopic diagnosis was hypertrophic gastritis; malignancy seemed to be definitely excluded.

This is a most instructive case. If the clinician were to have been guided only by the clinical history and the roentgen findings, the diagnosis of neoplasm most certainly would have

been made even after the second radiogram, taken after one month of medical management. Probably this patient would have been advised to have surgery and, in the presence of definite cardiac damage, the surgical risk was much greater than normal for a patient of his age. And, of course, an operative procedure would have been unnecessary.

This case further emphasizes the fact that while it is not always possible for either the gastroscopist or the radiologist to make a definite diagnosis on the first visit, the therapeutic trial and observation periods can be greatly shortened by using gastroscopy in conjunction with other methods.

**Case V.**—A thirty-four-year-old housewife whose *chief complaint* was "vomiting" (Fig. 67).

*Present Illness.*—The patient presented a rather bizarre type of history and had had vague abdominal pain of several years' duration. She had had an appendectomy for chronic appendicitis and "repair of right kidney hernia," without benefit so far as the abdominal distress was concerned. Subsequent hysterectomy and lysis of "adhesions" also failed to relieve the abdominal distress. Then the patient developed vomiting and this occurred after almost every meal. Frequent generalized headaches were a troublesome symptom.

*Physical examination*, including consultation with the ophthalmologist, revealed a definite eye muscle imbalance and convergence insufficiency to account for the headaches. There was deep, diffuse abdominal tenderness but no other positive findings. Proctoscopic examination revealed a fissure in ano.

The routine *laboratory examinations* were not significant. Stools were negative for ova and parasites. A two-hour fractional Ewald meal revealed the highest free hydrochloric acid to be 40 and the highest total to be 50. *Gastro-intestinal radiograms* were reported to reveal a normal gallbladder. The stomach was normal except for what appeared to be multiple, small filling defects in the pyloric area. The colon, except for spasm of the sigmoid portion, was negative.

A *gastroscopic examination* was done because of the filling defects reported on the radiologic examination, and because

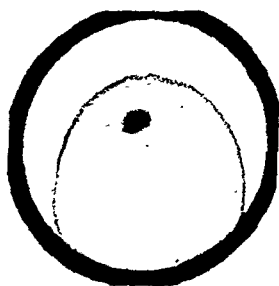
of the persistent vomiting. All parts were well visualized. The gastroscopic diagnosis was a normal antrum except for the linear hemorrhagic streak, thought to be due to vomiting or retching, and atrophic gastritis in the upper part of the stomach. The patient remained in the hospital for management for an irritable colon and, two weeks later, both the gastroscopic and roentgen examinations were repeated. Both examinations



A



B



C

Fig. 67.—A, Multiple small defects in antrum; B, normal antrum with mucous patches; C, normal antrum two weeks later (see Case V).

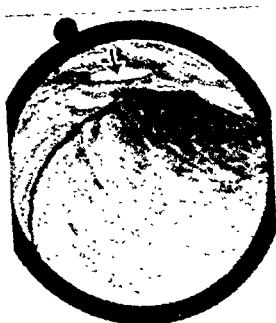
revealed a normal stomach and the patient's vomiting was considered to be due to a functional disturbance.

The gastroscopic examinations in this case were important because of the questionable filling defects in the pyloric area. It might well have been a malignancy or some other process which would be amenable to surgery or medical management but, by gastroscopy and subsequent radiographic examinations, it was established that the stomach was grossly normal.

**Case VI.**—A forty-six-year-old white steel worker whose chief complaint was "pain in the chest" (Fig. 68, A, B).



A



B



C



D



E



F

Fig. 68.—A, Duodenal bulb deformity without crater, stomach normal; B, benign ulcer in lesser curvature (see Case VI); C, suspicious ulcer niche in lesser curvature; D, typical benign ulcer; E, same case five weeks later; F, ulcer almost healed (see Case VII).

*Present Illness.*—For the past six years the patient had been subject to intermittent attacks of one or two months'

duration each year. The attacks were characterized by a retrosternal and lower chest pain of a burning nature, which was not related to activity and not accompanied by dyspnea or anxiety. There were no cardiorespiratory symptoms. Dysphagia and fulness due to gas were the only gastro-intestinal symptoms present. Occasionally hot milk would give relief from the pain.

*Physical examination* was essentially negative. Electrocardiograms failed to reveal evidence of cardiac disease. The glucose tolerance test was characteristic of diabetes mellitus. The blood count, urine, Wassermann and Kahn reactions were normal. Radiograms of the chest and esophagus were normal; however, the pyloric end of the stomach was spastic and there was an irregularity of the duodenal bulb due to an ulcer, but no definite crater was seen. An Ewald test meal revealed 35 units of free hydrochloric acid and 70 units of total acid.

*Gastroscopic examination* revealed a definite gastric ulcer in the lesser curvature near the angulus. The final clinical diagnosis was diabetes mellitus, an active gastric ulcer, and an old duodenal ulcer with questionable activity.

#### GASTRIC ULCERS

We believe that *every* gastric ulcer should be examined by *gastroscopy* and that the patient should have not one but probably *several* examinations. It is a well known fact that the gastric ulcer is more serious in many respects than the duodenal ulcer. It is also equally well known that from a single observation, the roentgenologist cannot say that the shadow he sees is the result of a benign or a malignant process. Therefore, the clinician should avail himself of every method at his command so that it can be established at an early date whether the ulceration is a malignant or benign process.

The old practice of placing the patient on ulcer management for a trial period of a month or six weeks and repeating the radiograms for evidence of healing or failure to heal as a therapeutic test for benign or malignant lesions is now antiquated. By direct visualization of the ulcer, the gastros-

copist is able to confirm the roentgen diagnosis of gastric ulcer. Of greater importance he can differentiate between benignancy and malignancy with a high degree of accuracy. And, just as important as the differential diagnosis, is the observation of the healing of an ulcer. It has been my experience in discussing this matter with other gastro-enterologists who are doing gastroscopy, that almost without exception they agree that one of the things they have learned from gastroscopy is to maintain a strict ulcer management for a longer period of time because the ulcer did not heal as fast as they had previously believed.

Careful studies by other workers have emphasized the need and the value of doing *both roentgen and gastroscopic examinations* to follow the course of the gastric ulcer. The ulcer may be seen only by the roentgenologist at one examination, whereas the gastroscopist only may see it at the next examination. Thus it requires both methods to be certain that the ulcer has been adequately visualized and each method can supply certain information which the other one cannot. In this way they are complementary and not competitive.

One of the frequent points of discussion concerning gastroscopy is about the gastroscopist's ability to *differentiate a benign from a malignant* ulceration. Those doing gastroscopy have contended that they see the stomach as no one else has an opportunity to observe it. The critic who believes that the gastroscopist cannot make the differential diagnosis with any more certainty than the surgeon or the pathologist forgets this important point: The specimen removed at the surgical table is a shrunken, devitalized avascular piece of tissue dissimilar to the stomach which the gastroscopist observes. Just as the roentgenologist is able to observe the stomach as a whole and to watch the peristalsis and motility, so the gastroscopist is able to watch the gastric walls change form and contour due to peristalsis, respiratory movements, and pulsations. Even more important is the coloring and appearance of the gastric mucosa and the lesion.

In the series of 246 cases examined at the Clinic, there

were satisfactory follow-up records on fourteen patients with benign gastric ulcers. The tabulation of the diagnosis by roentgenology and gastroscopy follows:

TABLE 1

Roentgenologist's diagnosis.	Gastroscopist's diagnosis.	Cases.
1. Indefinite diagnosis of "ulcer" or diagnosis uncertain and qualified, asking for further studies.	1. Benign gastric ulcer.	7
2. Carcinoma.	2. Benign gastric ulcer.	2
3. Qualified or questionable diagnosis.	3. Carcinomatous ulceration.	2
4. Qualified or questionable diagnosis.	4. Qualified or questionable diagnosis.	1
5. Normal stomach.	5. Benign gastric ulcer.	2

Because this series is too small to draw definite conclusions and to aid us in getting a more representative picture or a true cross section for comparison, another series of 118 cases which I had examined at the Los Angeles County General Hospital in the preceding year were reviewed. In that group of 118 cases, there were twenty-one in which we were able to have satisfactory follow-ups and we were convinced that the gastric disease was a benign ulcer. The cases were similarly studied and the following tabulation revealed the comparative diagnoses.

TABLE 2

Roentgenologist's diagnosis.	Gastroscopist's diagnosis.	Cases.
1. Diagnosis indefinite or qualified.	1. Benign ulcer.	10
2. Benign ulcer.	2. Benign ulcer.	5
3. Benign ulcer.	3. Questioned or qualified diagnosis.	1
4. Questioned or qualified diagnosis.	4. Ulcer not seen or examination not satisfactory.	4
5. Carcinoma.	5. Carcinoma.	1

It is apparent from these summaries that gastroscopy is a definite and valuable adjunct to the diagnostic method. In the total series, which represents thirty-five cases of benign gastric ulcer, the roentgenologist made the unqualified diagnosis of a benign ulcerating lesion on the first examination in only five instances. In each of these five instances, the gastroscopist was also able to make an unqualified diagnosis of a benign gastric lesion at the first examination. In contrast to this, however, there were a total of seventeen cases in which the roentgenologist made the diagnosis of "ulcer," and from the report the clinician had no hint or indication that the roentgenologist considered the lesion to be benign or malignant and the differential diagnosis rested entirely upon the clinician. Or, if the diagnosis of benign ulcer was made, it was qualified with the statement that the roentgenologist could not be certain about the lesion and so progress studies were indicated.

In this same group of seventeen cases, the gastroscopist was able at the first examination to make an *unqualified* or unreserved diagnosis of benign gastric ulcer. Of the remaining cases, it is interesting to note that in four instances the radiologic diagnosis was wrong while the gastroscopic diagnosis was correct. In two instances the radiologists made an unqualified diagnosis of neoplastic ulceration, while the gastroscopist made the diagnosis of benign gastric ulcer and, in the follow-up studies, it proved to be a benign lesion. In two other instances the radiologic examination had been negative, yet there were definite moderate-sized gastric ulcers observed during the gastroscopic examination. In contrast to these four cases, there were two others in which the radiologist made the diagnosis of an ulcerating process, but he could not be certain as to its benignancy or malignancy. However, the gastroscopist made unreserved diagnosis of ulcerative carcinoma and, in both instances, the lesion proved to be a benign process. It is also interesting to note that in one instance both methods were incorrect, and in one other instance neither the roentgenologist nor the gastroscopist could arrive at a definite diagnosis in the first examination.

**Case VII.**—A forty-five-year-old restaurant proprietor whose *chief complaint* was "abdominal distress" (Fig. 68, C, D, E, F).

*Present Illness.*—The first attack occurred in 1914 and was followed by subsequent attacks in 1918, 1923, and the present one in 1939. Each attack had been characterized by a dull, gnawing epigastric pain coming on three to four hours after eating, relieved by food or rest. The *physical examination* was negative. The routine blood and urine tests were normal. With an Ewald test meal the free hydrochloric acid reached a level of 50 and the total acid 72, forty-five minutes after the meal.

The *gastro-intestinal roentgen examination* revealed a normally functioning gallbladder without calculi, the duodenum was normal except for a diverticulum of the third portion, and the colon was spastic. The stomach, however, had a suspicious ulcer niche along the lesser curvature of the pars media.

The *gastroscopic examination* at that time demonstrated a typical, benign gastric ulcer on the angulus. Five weeks later the progress radiographic examination of the stomach reported a normal stomach and duodenum except for the diverticula of the third portion. However, at gastroscopic examination on the same day, a small gastric ulcer was still present on the angulus and there was a mild, superficial gastritis. Four months later, the examinations were repeated and a small, pin-head sized scar was seen gastroscopically, while the roentgen examination was negative.

**Case VIII.**—A forty-eight-year-old nurse whose *chief complaint* was "stomach trouble." (Fig. 69, A, B, C.)

*Present Illness.*—The patient had had distress intermittently for twenty years. It was characterized by bloating, belching, occasional sour regurgitations coming on half an hour after eating. At times there was relief from the use of soda and at other times a bowel movement would give relief. The patient used laxatives frequently. The *physical examination* was negative. Routine *laboratory data* were negative. The free hydrochloric acid reached a level of 35 units and the total

acid 46 units forty-five minutes after the administration of an Ewald meal.

The first *roentgen examination* revealed a normal gallbladder and duodenum. The colon was typical of a spastic or

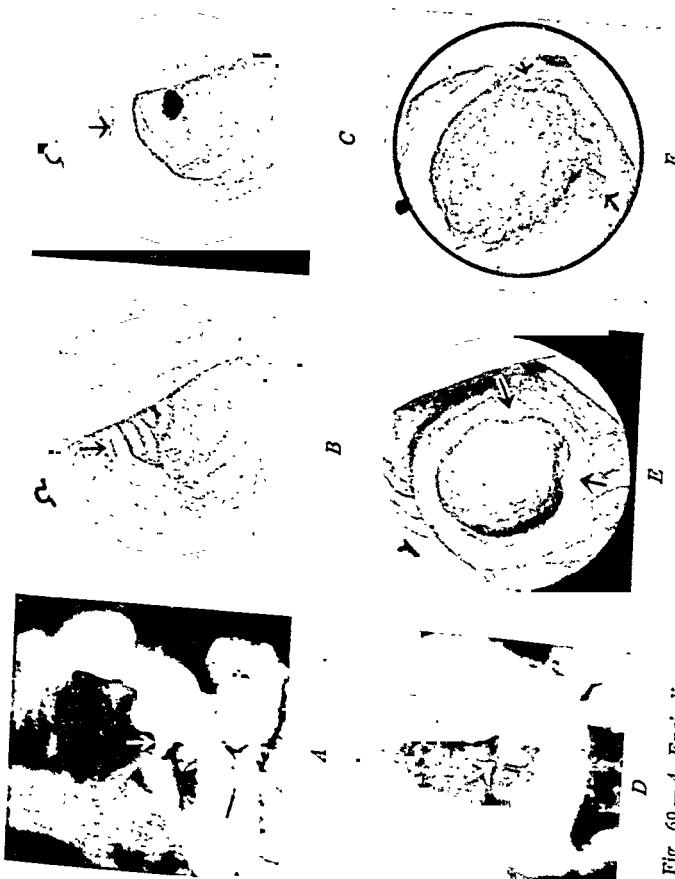


Fig. 69.—A, Encircling type filling defect of antrum; B, small gastric ulcer, entire antrum including lesser curvature visualized, no evidence of carcinoma; C, ulcer almost healed after three weeks of treatment (see Case VIII); D, large ulcer in lesser curvature with raised edge, note nodular appearance at 3 and at 6 o'clock; E, large ulcer; F, definite evidence of malignancy (see Case IX).

irritable colon, the left half being spastic and the right half being atonic. However, there was reported an encircling type of filling defect in the pars pylorica due to neoplasm.

At *gastroscopic examination*, three days later, the entire

stomach was well visualized. The antrum appeared lumpy and thickened and no peristalsis other than one or two very shallow waves was noted. At the lesser curvature of the body a benign gastric ulcer was seen. The gastroscopic diagnosis was benign gastric ulcer on the angulus and severe hypertrophic gastritis. The patient was placed on ulcer management and three weeks later the roentgenograms were repeated and reported to be normal. At gastroscopy, however, the ulcer was still visualized and this time there was excellent visualization of the entire antrum and there was definitely no evidence of malignancy. Final gastroscopic examination was done five weeks later at which time a small, yellowish-white scar at the site of the ulcer was found.

**Case IX.**—A forty-six-year-old housewife whose *chief complaint* was "pain in the stomach." (Fig. 69, D, E, F.)

*Present Illness.*—This began three years previously with epigastric distress of varying character. The pain usually occurred one to four hours after eating and was relieved by food and alkalies. In the past year the distress had become more persistent and more severe, and on one occasion the patient had vomited some blood. The appetite had been poor and, during the three-year period, there had been a 25 pound loss of weight. This, however, was attributed to the fact that the patient's distress first came on following her husband's death in an automobile accident and it was thought that there was a functional element which prevented the patient from getting adequate nutrition. *Physical examination* was negative except that the patient, an Italian woman, was obese and extremely apprehensive and nervous. The routine *laboratory tests* of blood and urine were negative. The Ewald test meal revealed 37 units of free hydrochloric acid and 55 units of total acid forty-five minutes after the meal.

The *gastro-intestinal roentgen examination* revealed normal duodenum and colon, but there was an ulcer crater in the pars media of the stomach. The diagnosis of ulcer, however, was not qualified and the radiologist did not state that it might

be either benign or malignant. At *gastroscopy*, a definite ulcer crater was visualized and it was thought to be a benign gastric ulcer. It was reported that the ulceration was well-defined, although it was a bit irregular in two places, one of which showed small hemorrhagic changes. The entire crater rested in a large elevation and gave the appearance of a doughnut or a thickened ring about the crater. The patient was advised to enter the hospital for strict ulcer management and progress studies, but she refused to do this. After one month of ulcer management at home the patient returned for progress examination and, at that time, by *gastroscopy* the ulcer appeared to be a little bit smaller, although it was of the penetrating type and seemed to rest in a tumor-like elevation. However, the process was still considered to be a benign lesion and, since the patient could not have her progress roentgen examination that day, it was not insisted upon.

The patient was allowed to return home and was not seen for six weeks' time, when another *gastroscopic* examination was done and at that time the ulcer appeared the same as it had on the two previous examinations. Still the patient refused to enter the hospital and the lesion was still considered benign by the *gastroscopist*. Two months later the lesion appeared to be about the same and the patient refused to enter the hospital for surgery. It was not until three months later after persistent pain unrelieved by the usual ulcer medicaments that the patient finally entered the hospital. The day before operation the *gastroscopic* examination was repeated and the ulcer crater was well visualized. Although it showed evidence of malignancy, it was, after considerable discussion, considered to be a benign lesion.

It is interesting to note here that the pathologist considered the ulceration to be a benign process when he examined the surgically resected specimen. This is an important point, especially for those critics who contend that one cannot make the differential diagnosis between a benign and malignant lesion by *gastroscopy*. It is apparent from the drawings of the lesion made at the time of examination (see Fig. 69), and it is

equally apparent from the description of the lesion in each of the gastroscopic examinations that the process was a malignant one. The fault was not with the method but with the gastroscopist's interpretation of the lesion.

#### GASTRIC CARCINOMA

Patients known or *suspected* of having a gastric carcinoma constitute another important indication for gastroscopy. We believe that *all* patients in this group should have a gastroscopic examination. It is important that the roentgen and clinical diagnoses be confirmed by the gastroscopic examination. It may also be helpful to the surgeon to know the approximate mucosal extent of the lesion so that he may have more definite plans for operation before the surgical exploration.

Furthermore, we believe that patients having had the gastric operation, or roentgen therapy, or both, for carcinoma of the stomach should have periodic roentgen and gastroscopic examinations, for it is by these means that we may be able to detect early recurrences or follow the effects of radiation therapy. We suggest that these patients be examined *at least every six months* even though they may be entirely free of symptoms.

Comparison of the roentgen and gastroscopic findings in the Cleveland Clinic and the Los Angeles series was also made. In the Clinic series there were twelve malignancies, of which seven were the ulcerating type and five the nonulcerating type. In the Los Angeles series there was a total of twenty-four malignancies, of which four were ulcerating and twenty were without ulceration.

In the Clinic series, the radiologist made the diagnosis of an ulcerating carcinoma and the gastroscopist made the same diagnosis in four cases. In one instance the radiologic diagnosis was qualified or uncertain while, at gastroscopy, the diagnosis of an ulcerative carcinoma was definitely made. In another instance the radiologic diagnosis was ulcerative carcinoma and the lesion was not seen at gastroscopy, so that no diagnosis

could be made. In one other case, the diagnosis was uncertain by both methods. In the Los Angeles series, the correct diagnosis was made by both methods in two instances. In one case the roentgen diagnosis was uncertain, while the gastroscopist was incorrect in making the diagnosis of a benign gastric ulcer. It can be seen from these cases that both methods are about equally reliable in the diagnosis of rather advanced ulcerating malignancies.

When we consider the nonulcerating lesions of the four Clinic cases, three were correctly diagnosed at the first examination by both methods. In one instance the roentgen diagnosis was infiltrating carcinoma and the gastroscopic diagnosis was uncertain and qualified. In the Los Angeles series there were twenty cases, of which eight had been diagnosed correctly by both methods at the first examination. In one instance the roentgen diagnosis was correct while the gastroscopic diagnosis was uncertain. However, in two cases both methods were unable to make the diagnosis at the first examination. In three instances, the gastroscopist was able to make the definite diagnosis when the roentgenologist was not able to. In one case the roentgen diagnosis was uncertain while the gastroscopic diagnosis was carcinoma. In another case the roentgen diagnosis was benign ulcer and spasm while the gastroscopic diagnosis was carcinoma, and in the third case, the radiologic diagnosis was negative and the gastroscopic diagnosis was carcinoma.

**Case X.**—A fifty-five-year-old machine operator, whose *chief complaint* was "lumps in the neck." (Fig. 70.)

*Present Illness.*—For three months the patient had noticed a painless swelling in both sides of the neck which had gradually increased in size. Three weeks prior to admission he first noticed in the epigastrium a mass the size of an egg. Other than the presence of these masses, the patient had no swellings. *Physical examination:* Temperature 99.8° F., pulse 134 beats per minute. The patient was pale and there was pitting edema of the lower extremities. There were rubbery,

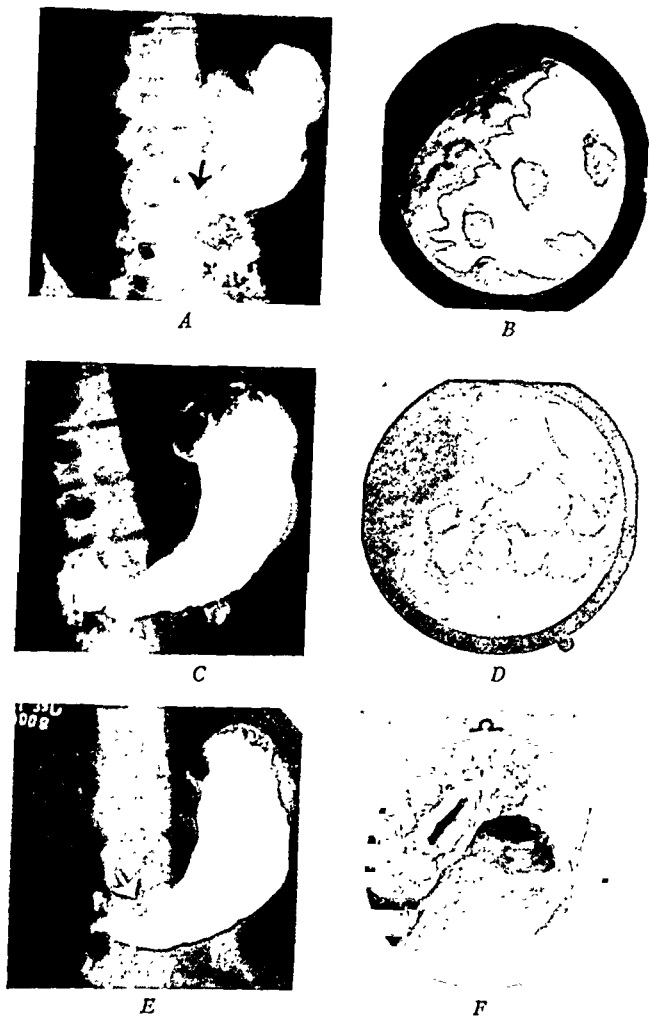


Fig. 70.—*A*, Large filling defect in pylorus of stomach; *B*, portion of posterior wall showing infiltration and neoplastic nodules and pathologic exudate; *C*, no filling defect but fluoroscopic evidence of infiltration eight weeks later after roentgen therapy; *D*, gastroscopic appearance unchanged; *E*, recurrence of filling defect nine months later; *F*, extensive infiltration with large ulcer on angulus (see Case X).

discrete fixed glands in both sides of the neck. A firm smooth epigastric mass descended with respiration. The liver edge

was sharp and it was felt at the level of the umbilicus. Systolic blood pressure was 130 mm. of mercury and the diastolic 100 mm. of mercury. Cardiac findings, however, were normal. The usual *laboratory examinations* were normal.

*Roentgen examination* of the gastro-intestinal tract revealed a large filling defect in the pyloric portion of the stomach with a smaller defect in the cardiac portion which was thought to be due to neoplasm.

Two weeks later, on December 22, 1938, the first *gastroscopic examination* was done. The lower two-thirds of the stomach was involved with a bizarre type of infiltrating, nodular lesion. The gastroscopic diagnosis, partly on the basis of the gastroscopic findings and partly on the basis of the clinical improvement, was lymphosarcoma of the stomach.

The next progress studies were done on February 6, at which time the roentgenologist reported no filling defect but some infiltration in the wall of the pyloric and mid-body regions. The following day, at gastroscopic examination, the stomach appeared essentially as it did in the previous examination, with the additional finding of atrophy on the upper anterior wall which was thought to be due at that time to the roentgen therapy.

Several months later a mediastinal mass developed and this responded in a few weeks to radiation therapy and completely disappeared. At that time, in August, 1939, a radiogram of the stomach was normal. No gastroscopy was done at that time. The patient was next seen in October, 1939, when a gastroscopic examination revealed an ulcerating, infiltrating, nodular process in the lower third of the stomach. The same day, following gastroscopic examination, the radiographic examination was repeated and an irregularity and filling defect along the lesser curvature was found. Roentgen therapy to the stomach was again given, but insufficient time has elapsed to warrant recheck roentgen and gastroscopic examinations. In the meantime, however, the patient developed nasal distress and otolaryngologic examination revealed what was thought to be a primary lymphosarcoma in the nasopharynx. A biopsy

of one of the neck glands when first seen was reported to be typical of lymphosarcoma.

**Case XI.**—A forty-eight-year-old railroad foreman whose chief complaint was "stomach trouble." (Fig. 71.)

*Present Illness.*—This patient's stomach trouble dated back nine years. At first the patient complained of dull, epigastric pain coming on one-half hour after eating and relieved by alkalis. He would be distress-free for a period of several weeks at a time. In the past six months, however, the symptoms had been more severe and more persistent and there had

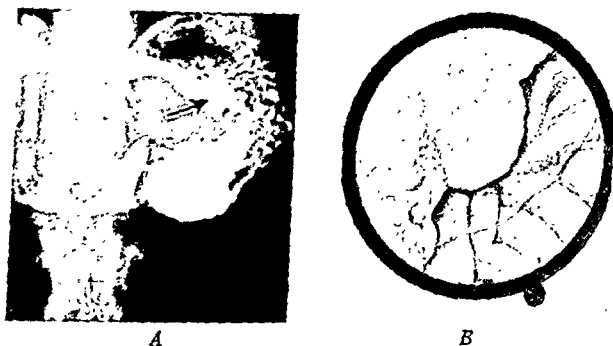


Fig. 71.—A, Extensive infiltration of upper part of pars media; B, extensive nodular polypoid carcinomatous infiltration; string of mucus crossing over posterior wall (see Case XI).

been little or no relief from the use of alkalis. With the increase in distress there had been a 20 pound loss of weight.

*Physical examination* revealed slight emaciation but no other significant findings. There were no abdominal masses nor tenderness on palpation. The usual *laboratory examinations* were normal.

*Roentgen examination* of the gastro-intestinal tract revealed an extensive infiltration in the upper part of the pars media of the stomach. The *gastroscopic examination* revealed a nodular extensive infiltration in the upper mid-portion of the anterior wall and lesser curvature. At one place there was a

polyp-like protrusion into the gastric lumen. Scattered throughout the infiltration were what appeared to be cystic or gelatinous masses. The diagnosis was carcinoma of the stomach. The infiltration extended to the cardiac orifice and from the gastroscopic standpoint the lesion was considered inoperable. At operation these findings were confirmed and sections made from biopsy of an omental node revealed adenocarcinoma.

### GASTRIC OPERATIONS

The next group of patients who should have gastroscopic examinations are those who have undergone any type of gastric operation, whether it be gastro-enterostomy or partial resection, for a benign or a malignant lesion. It is well known that many patients having had an enterostomy or partial resection will frequently have continued distress or will be free of trouble for a long period, only to have it recur. The distress may be typical of ulcer, or not infrequently it is an atypical type of distress. It is equally well known that it is not always easy to demonstrate marginal or jejunal ulcers.

On the other hand, the gastroscopist is usually able to see almost all of the gastric mucosa and is usually able to see the stoma. If the stoma is seen, an ulcer situated at or near its margin would also usually be well seen. The direct visualization, then, of the stoma and an ulcer, if present, by means of gastroscopy, becomes a valuable adjunct to the diagnostic methods. I have seen two very instructive cases of marginal ulcers. In one case the ulcer had been demonstrated radiologically and by gastroscopy. However, when the patient was operated upon following these examinations, the surgeon was unable to demonstrate the ulcer. Likewise, the ulcer was not demonstrable in the gross specimen removed when the enterostomy was undone. It was not until the tissue was placed under water and carefully teased out that the crater was demonstrated. The second case is even more interesting, in that the ulcer had not been demonstrated radiologically but had been visualized gastroscopically. In this instance the ulcer was not demonstrable in the gross resected specimen with cer-

tainty even when carefully teased out; however, serial sections revealed definite microscopic evidence of peptic ulceration.

Not all patients will have marginal ulcers in spite of the fact that they have persistent abdominal distress, which may or may not be of the ulcer type. Gastritis, occurring in gastro-enterostomized or partially resected stomachs, is fairly common. It is frequently a severe type of gastritis with erosive manifestations. In such cases the true condition of the stomach and the cause of the patient's symptoms will be revealed only when gastroscopy is used in conjunction with radiologic examinations.

**Case XII.**—A forty-five-year-old dye maker whose *chief complaint* was "pain in the stomach." (Fig. 72, A, B.)

*Present Illness.*—Twenty years previously this patient had had a gastro-enterostomy for duodenal ulcer. For fifteen years he was symptom-free, but for the past five years had had recurring intermittent attacks of pain, characteristically localized to the epigastrium and coming on two hours after meals. The pain was relieved by the taking of food or soda. At times he had passed what he described as "tarry stools."

*Physical examination* was essentially negative except for some epigastric tenderness. The usual *laboratory data* were normal. Stool specimens for examination for blood could not be obtained.

The first *radiographic examination*, in June, 1937, revealed a large penetrating gastric ulcer in the lesser curvature. Three weeks later progress examination revealed that the ulcer niche was at least a third smaller. By October the ulcer had not decreased further in size. However, the following March, 1938, no niche was present. In July, 1939, the patient returned because of recurrent distress. At that time roentgen examination was reported to show a normally functioning gastro-enterostomy with no demonstrable evidence of gastric ulcer other than convergence of folds at the pars media which was the location of the ulcer previously noted.

At *gastroscopic examination*, however, a definite gastric ul-

cer in the hub of the converging folds was seen; associated with this was a marked deformity of the stomach due to the scarring and radiating folds. There was also severe gastritis.

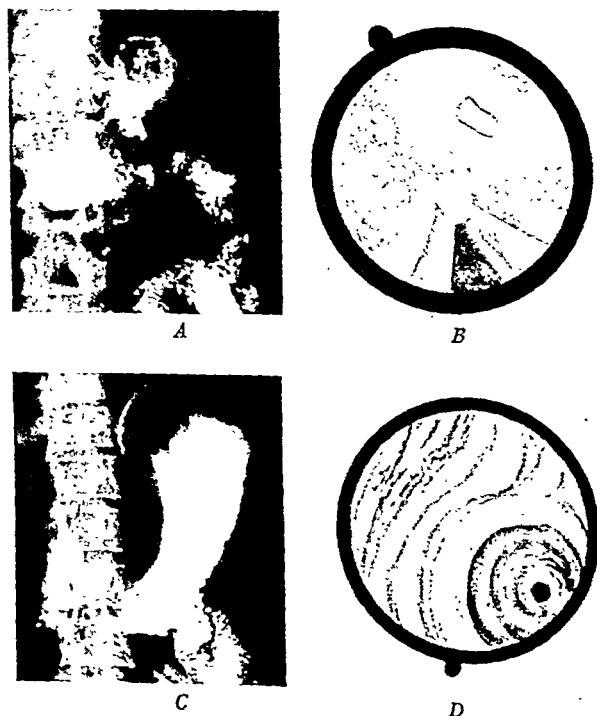


Fig. 72.—*A*, Normally functioning gastro-enterostomy, with no demonstrable evidence of gastric ulcer; *B*, ulcer crater on posterior wall portion of stoma with convergence of folds to apex and pseudopolypoid formation (see Case XII); *C*, normally functioning gastro-enterostomy; *D*, gastritis of post-operated stomach with normal stoma and jejunum.

The value of the gastroscopic examination in demonstrating the ulcer in this case is apparent.

**Case XIII.**—A thirty-seven-year-old nun whose *chief complaint* was "pain in the stomach, nausea, and vomiting." (Fig. 72, *C*, *D*.)

*Present Illness.*—The onset of the present illness dated to

1925 at which time the patient had definite ulcer distress and obtained almost complete relief with medical management for five years. The distress returned, however, and gastro-enterostomy was advised. Following the operation she was completely free of distress for four years, but then began to have recurrent attacks of severe epigastric pain associated with nausea and vomiting. For the past five years these attacks had occurred two to five times a year and were becoming progressively more severe. They were occasionally associated with tarry stools and small hematemesis.

*Physical examination* was negative except for moderate epigastric tenderness.

*Laboratory examinations* revealed 3,980,000 erythrocytes, with 78 per cent hemoglobin and 5,400 leukocytes. Urine specimens were negative. The blood sugar level was 88 mg. per 100 cc. Blood Wassermann and Kahn tests gave negative reactions. With the ordinary Ewald meal the free hydrochloric acid at the end of forty-five minutes was 20 and the total acid 41. Biliary drainage on two occasions revealed findings suggestive of cholangitis.

The *roentgen examination*, however, revealed with oral cholecystographic dye a normally functioning gallbladder without evidence of calculi. It also revealed a normally functioning gastro-enterostomy and irregular duodenal bulb. The colon was normal.

Three months later a progress roentgen examination revealed the same findings except that the duodenum was normal. The patient, however, was still having distress.

At the time of the first roentgen examination *gastroscopy* revealed a severe gastritis involving all of the stomach. The stoma was well seen and there was no evidence of marginal or jejunal ulcer.

In this case gastroscopy was of value in that it confirmed the roentgen diagnosis of a normally functioning enterostomy without evidence of ulcer, because the stoma was well visualized and the few centimeters of the jejunum were seen. It is quite likely that the patient had a recurrence of the duodenal

ulcer as evidenced by the irregular duodenal bulb and a subsequent normal bulb. However, she also had a severe gastritis which did produce severe gastric distress.

### CONCLUSIONS

Gastroscopy is a valuable adjunct to other methods for diagnosis of gastro-intestinal conditions. The established *indications* are:

1. Patients with negative roentgen gastro-intestinal findings but in whom one still suspects the presence of gastro-intestinal disease.
2. Patients with inconclusive, inconsistent, or inadequate roentgen findings.
3. Patients in whom a gastric ulcer has been demonstrated radiologically.
4. Patients in whom gastric carcinomas have been demonstrated radiologically.
5. Patients who have had any type of gastric operation for either a benign or a malignant lesion. In the latter case examinations should be done at least every six months.



## THE TREATMENT OF PERIARTHRITIS OF THE SHOULDER

JAMES I. KENDRICK

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THE important part which the muscles and ligaments play in the stability and function of the shoulder joint make these structures the most common site for pathologic changes causing pain and disability in the joint. The wide range of motion in the joint makes the periarticular structures particularly susceptible to injury.

The economic importance of the painful shoulder has resulted in exhaustive study by the anatomist, pathologist, clinician and surgeon. This wide scope of investigation has given us the information with which to arrive at the cause of the difficulty and to plan the treatment.

The clinical picture of scapulohumeral periarthrititis was described by Duplay in 1872 and was later referred to as "Duplay's disease." The later reports of Codman,<sup>1</sup> however, would establish scapulohumeral periarthrititis as a stage in a disease process rather than a disease in itself. I would be inclined to agree with Douthwaite<sup>2</sup> that scapulohumeral periarthrititis arises probably as a subacromial bursitis with extension of inflammation to the subdeltoid tissues, resulting in fixation of the shoulder joint and pain.

I wish to mention briefly the acute processes, as I will describe in detail the treatment of the chronically fixed or frozen shoulder. I do wish to discuss also the acute stage in so far as its treatment has a definite bearing upon the *prevention* of the chronic stage. In our experience the acute stage has been easier to treat, hence the prevention of fixation would be compared to prophylactic measures used in the prevention of typhoid, smallpox, etc.



of the acute type. Duplay described the outstanding symptoms and physical findings.

The outstanding symptom is *pain*, and so often this pain is *severe* and present *at night*. The pain is described differently by various patients, but it often is in the region of the deltoid insertion and is described as "radiating into the forearm and the side of the neck." Limitation of movement is of secondary importance. *Abduction* and the *rotations* are most markedly limited and these movements are painful. In my experience, the rotations are the motions most limited and attempt at these motions causes considerable pain. *Flexion* and *extension* are free and painless through a fair range of motion, and this point is of importance in differentiating limitation in motion from intra-articular conditions. By deep palpation, *tender areas* are often found over the greater tuberosity and in the region of the deltoid insertion. *Muscular wasting* about the shoulder, as evidenced by deltoid and supra- and infraspinatus atrophy, completes the picture. These patients show in a general way just what they have been through. They have lost weight, they have lost sleep and their fortitude has been taxed. These factors have to be considered when their treatment is outlined. In observing these patients during treatment we have come to feel that their pain is directly related to the limitation in motion, as evidenced by the departure of pain as the range of motion improves.

In operations about the shoulder much of the *pathology* has been observed, but not as completely as in a case reported by Duplay: This was the case of a fifty-three-year old man who died of pneumonia and whose shoulder was examined at necropsy. The shoulder had been manipulated two months before his death. On the affected side the deltoid was paler than normal; the subdeltoid tissue was fibrous, exhibiting dense bands running to the upper end of the humerus. The sub-acromial bursa was obliterated. The tendons of the supra- and infraspinati had lost their polish as had also the inferior surface of the acromion. It was evident that subacromial bursitis was the chief lesion, with extension to neighboring struc-

**Acute Stage.**—In referring to the acute processes, I make especial reference to the acute *sprains* of the shoulder and to acute *subacromial bursitis*. *Trauma* so often gives the entire basis for the development of either, but so very frequently *exposure* or a *focus of infection* has a bearing upon the beginning of a subacromial bursitis. Attention to the patient's *general condition* and to *foci of infection* cannot therefore be ignored and is of equal importance with the local treatment. Sprains, in so far as the tendons of the short rotators may be injured, have mounted in importance and deserve careful consideration from the examiner. The mild sprain may require bed rest, with traction and abduction to promote the patient's comfort. The pain in acute subacromial bursitis is very severe and *bed rest* is almost essential. *Abduction* of the arm and the application of a few pounds of *traction* will in most cases give immediate relief. The application of *moist heat* during the first several days gives the most relief. This may be followed by *infra-red baking*, and later, *diathermy* of low intensity.

It has been shown that in the acute cases of bursitis there is often considerable distention of the bursa and that this distention is the cause of the severe pain. From the results of Weeks and Delprat,<sup>3</sup> obtained from *needling the bursa*, and from the results of Patterson and Darrach,<sup>4</sup> obtained from needle irrigation of the bursa, and from our experience, I would feel that this simple surgical procedure was the treatment of choice, especially in those cases not relieved promptly by traction and physiotherapy. If one of these procedures is not effective, *operative incision* should be resorted to. In all cases I feel that a full range of motion should be executed passively each day and this is usually not difficult, especially after the muscle spasm is overcome by a short period of traction.

**Chronic Stage.**—Regardless of the type of treatment used during the acute process there will be some who will have some *fixation*, and there will be those cases which received no treatment and who seek help for their pain and their fixation. During the past two years we have had more of this type than

position of 90 degrees abduction and 90 degrees external rotation. The extreme positions of external rotation are not necessary and only make the patient more uncomfortable after the manipulation and more apprehensive when beginning passive and active movements. This light traction applied following manipulation has been so important in the patient's comfort



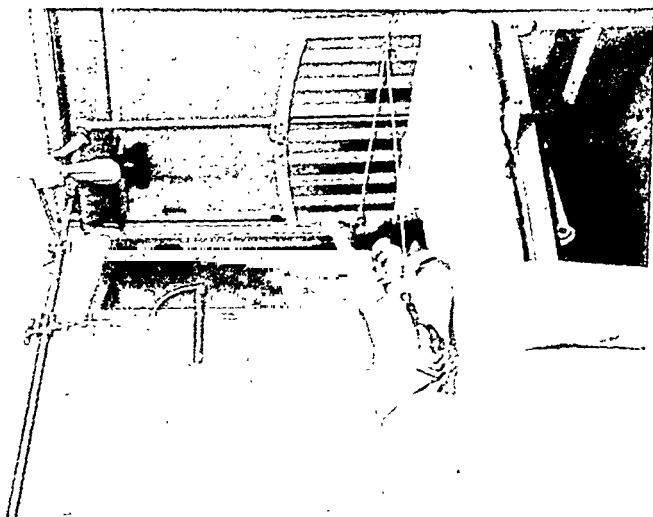
Fig. 73.—The traction apparatus.

that we have come to feel it is essential. Three to 5 pounds of traction in abduction and sufficient weight to suspend the hand and maintain 90 to 115 degrees of external rotation should be used.

*Ice caps* should be applied to the shoulder during the first twenty-four to forty-eight hours following manipulation. During the first two days following a manipulation, a *complete*



Fig. 74.—Apparatus used for exercising the shoulder.



*range of motion should be executed passively.* There is usually no difficulty and little pain is experienced from the movement. On the third day, *physiotherapy* should be started. *Diathermy* of low intensity can be used, and following this, *active movements* should be started.

On the fourth day, the *exerciser* should be attached to the head of the bed (Fig. 74). This exerciser can be made from two pulleys, a piece of rope and two hand grips. The exerciser is helpful in encouraging active movements, as the sound arm helps to lift the manipulated arm into abduction and external rotation. *Traction* should be reapplied after each treatment and should be used constantly during the first week.

At the end of one week, the patient can be allowed out of bed for short periods. During the final few days in the hospital *more active exercises* should be added, such as wall-climbing with the fingers, placing the hands behind the head and behind the back, etc. After ten days to two weeks the motions may not be entirely free because of muscular weakness, but usually, passively, a full range of motion can be obtained without much discomfort. After hospital discharge, the patient should be kept under close observation and the *physiotherapy* and *exercises continued until a full range of motion is present*.

In considering the duration of symptoms and the chronicity of this condition, it should not be expected that the return to function will be immediate. Before a normal range of motion is possible there must develop improved strength in the atrophied muscles. There is improvement in the pain rather promptly, but only with time and persistence does the strength return.

**Summary.**—In conclusion I should like to encourage careful study and investigation of the patient with periarthritis of the shoulder. Dickson and Crosby<sup>5</sup> have pointed out the importance of foci of infection and glandular dysfunction in these patients. I agree that the general treatment of the patient is of equal importance with the local treatment. I suggest treatment for all of the factors—*eradication of foci, regulation of the diet, and systematic heliotherapy*—so as to give the patient the advantage of a generally improved physical condition. I have outlined the local treatment in detail, as the use of *traction* and the *exerciser* has helped to make the patient more comfortable, to gain his cooperation, and to make the treatment more effective.

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## THE USE OF NICOTINIC ACID AND THIAMIN CHLORIDE\* IN THE TREATMENT OF MÉNIÈRE'S SYNDROME

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A GREAT many articles have been written on Ménière's syndrome, yet conflicting views still exist as to its etiology, pathology, diagnosis, and treatment. The terminology alone speaks for the confusion that accompanies this disease, as the terms "Ménière's syndrome," "Ménière's disease," and "Ménière's symptom complex" are used synonymously. Since almost every author has his own conception of Ménière's syndrome, it becomes quite important that each one state his diagnostic criteria.

**Diagnosis.**—The diagnosis is not particularly difficult if certain characteristic symptoms are kept in mind:

1. Sudden onset of attacks of rotational *vertigo*.
2. *Deafness* of the perceptive type, usually more marked in one ear and always progressive.
3. *Tinnitus*, which is more marked in the ear with the greatest hearing loss.
4. *Nausea* and *vomiting*, usually present, depending on the severity of the attack.
5. The attacks come at *irregular intervals* and *recur* with increasing frequency and severity.
6. Aside from the tinnitus and deafness, the patient is *perfectly well between attacks*.

The attacks vary in intensity from a mild swimming sensation of the patient himself or of the surrounding objects, to that of rapid spinning or lateral pulsion. The attack may begin without warning, or may be preceded by increased tin-

\* Thiamin chloride was supplied through the courtesy of Merck and Company.

nitus and accompanying diminution of hearing. The vasomotor symptoms also depend on the intensity of the spell, varying from pallor of the face to nausea and vomiting and dimness of vision, but they are never accompanied by convulsive movements.

Occasionally a patient will describe the sensation of objects moving up and down, that he will fall forward or backward, or that the floor comes up to meet him. This type of case may result from a disturbance in the saccule. However, such a case is rare and is not included in this group of case reports.

The vestibular tests have no value in the diagnosis or prognosis of Ménière's disease. Spontaneous nystagmus during an attack will also vary; it may be towards or away from the affected ear and in severe cases reaches a third degree.

The type of vertigo must be carefully elicited from the patient, and the history alone will usually differentiate between vertigo of ocular origin and that of aural origin. The ocular conditions causing vertigo are chiefly those of muscle imbalance, diplopia and refractive errors, or any condition in which stereoscopic vision is interfered with.

**Etiology.**—The etiologic factors which produce this syndrome are multiple:

1. *General systemic conditions*, such as anemia, leukemia, cardiac disease, renal disease, gastro-intestinal disease, arteriosclerosis, drugs, tobacco, and foci of infection.

2. *Aural conditions* causing vertigo. Otitis media and blocking of the eustachian tube may cause vertigo, which is relieved by inflation; also stricture of the eustachian tube without otitis media may be a cause. Vertigo may occur in the presence of chronic suppurative otitis media and is an indication of perilabyrinthitis or labyrinthitis which requires immediate attention.

3. *Allergy* is believed by several authorities to be an etiologic factor; however, if this were true, one would expect it to occur more often in recognized allergic states such as asthma, urticaria, migraine, seasonal and perennial rhinitis.

4. The *idiopathic* causes, however, comprise the majority of cases of true Ménière's syndrome.

**Pathology.**—Our knowledge of this disease rests mainly on clinical observations. It was in 1861 at the Imperial Academy of Medicine of France that Prosper Ménière<sup>1</sup> delivered a paper entitled "Memoir Concerning Lesions of the Internal Ear Giving Rise to Symptoms of Cerebral Apoplectiform Congestion." This was the first time that the syndrome of deafness and tinnitus accompanied by attacks of vertigo, vomiting, and nystagmus had been related to the inner ear. Included in his paper was an autopsy report, resulting in generations of medical students being taught that these attacks were due to a hemorrhage into the labyrinth. As we study Ménière's type of patients it does not seem possible that their symptoms result from intralabyrinthine hemorrhage in a very high percentage of cases.

In an excellent article by Crowe,<sup>2</sup> based on a study of 117 patients, the lesion is localized anatomically to one of two areas: First, that portion of the eighth nerve trunk where the cochlear and vestibular nerves come together and are contained in one sheath; a common lesion at this site is the acoustic tumor. The second possible anatomic location of the lesion is in the inner ear; even though Corti's organ and the vestibular end organs are widely separated, they have one property in common, namely, the endolymph. Any change in the physical or chemical properties of this fluid which fills the membranous labyrinth can affect both the cochlear and vestibular end organs.

Clinically, we can localize the lesion by reproducing the attacks with the caloric test; also severing the eighth nerve will relieve the attacks. Therefore, we can say that the lesion is located in the *labyrinth*. Mygind and Dederich<sup>3</sup> of Copenhagen believe that the symptoms are due to faulty water metabolism, giving rise to increased endolymphatic pressure.

Furstenberg, et al.<sup>4</sup> state that the symptoms are due to the abnormal retention of sodium in the body.

Hallpike and Cairns<sup>5</sup> report the autopsy findings on two

patients who died after section of the eighth nerve for relief of vertigo. They found gross dilatation of the saccule and scala media with obliteration of the perilymphatic cistern and the scala vestibuli. There was degeneration of the stria vascularis, Corti's organ, also degenerative changes in the epithelium of the macula and crista. The perisaccular connective tissue around the saccus endolymphaticus was absent, and Reissner's membrane was displaced to the wall of the scala vestibuli. The authors are led to believe that in Ménière's syndrome, there is increased endolymphatic pressure due to increased secretion or diminished absorption of endolymph. This is the first complete histologic study of cases of true Ménière's syndrome to be reported in the literature. The previously reported cases have been incompletely studied histologically (sections of the eighth nerve only) or were not true idiopathic cases but were secondary to some unusual disease as in the case of a neurofibroma located in the basal coil of the cochlea described by Wittmaack and a case of generalized encephalitis of traumatic origin described by Videbeck. The essential pathologic change, extreme dilatation of the endolymph space must be regarded as the end result of the condition, but why the endolymphatic pressure should increase remains unknown.

**Treatment.**—The Furstenberg management, consisting of a low sodium, salt free diet supplemented with large doses of ammonium chloride, is rather strenuous treatment and in our hands not too successful. *Surgical* section of the vestibular nerve is obviously radical therapy and not without danger to life. Furthermore, this disease is not unilateral in the high percentage of cases that we have been led to believe. Neurosurgeons have placed a "halo" about one ear, probably in an unconscious attempt to simplify surgical indications for treatment.

As we studied people with this disease, we were impressed with their peculiar *dietary* habits. Usually they were almost all vegetarians or carbohydrate addicts. There was apparently an inadequate intake of protein in the majority, and in those

who did eat meat or meat products, we noted the complete absence of teeth, the loss of molar support, or the use of dentures. Those wearing dentures usually gave the history of having had many teeth removed prior to obtaining their dentures so that the masticating power of the patient was definitely deficient over a long period of time. Merely asking a patient if he is on a regular diet is not adequate. To the average patient a regular diet may mean anything from coffee and doughnuts to alcoholic spirits. An insight into the patient's diet can best be obtained by having him enumerate the foods he ate the previous day or days.

The association of perceptive deafness with this syndrome is also significant. This association, along with the age incidence and progressive nature of the disease is suggestive of a *degenerative* process. It is well known among those who treat pellagra that a high percentage of pellagrins have rotational vertigo. Our observations regarding these patients' nutritional deficiency and the belief by Selfridge<sup>6</sup> that perceptive deafness is a deficiency disease prompted us to use nicotinic acid and thiamin chloride in the treatment of this disease.

Approximately three years ago we tried large doses of thiamin chloride, orally and parenterally, without appreciable benefit. A few months later we tried nicotinic acid, but it was not until eight months ago that we tried the two together and obtained beneficial results. Since using this form of therapy, twenty cases of Ménière's syndrome have been treated. Seventeen of the twenty patients are entirely free from their vertigo and, in the remaining three, the vertigo is markedly improved, so that they are able to carry on with their occupations. Ten of the twenty patients are free from their tinnitus and in the remaining ten, the tinnitus is barely audible. In twelve cases there was definite improvement of hearing and these included all the cases that obtained relief from their tinnitus. In the remaining eight cases, the hearing remained stationary. Most of the patients were treated for from two to three months before complete relief was obtained. In eight cases definite improvement was noted in two weeks; in twelve, improvement

was not noted until approximately six weeks after beginning treatment. The improvement following treatment was gradual. The patient would continue to have his attacks of vertigo for several weeks, but the attacks became less and less severe with longer remissions until they reached the stage where they had the sensation of an impending attack, which never came, and finally, there was disappearance of the vertigo altogether. This method of subsidence of attacks is very much against spontaneous remission.

In a spontaneous remission the attacks do not taper off gradually but there is usually a sudden complete subsidence in such a remission. Furthermore, during the first two months, withdrawal of this treatment will reproduce the attacks.

Various sized *doses* were tried, and at the present time we are using 250 mg. of nicotinic acid per day, given in five divided doses. The thiamin chloride is given in 10 mg. doses twice a day. *Oral* administration seems to be as effective as the parenteral method. The patient is kept on this treatment until he is free from his attacks; usually this does not exceed three months. The redness, flushing and burning of the skin which sometimes occur following the administration of nicotinic acid are not contraindications to its use. The patient should be warned that such symptoms may occur in order to prevent undue alarm.

This treatment is *supplemented* with a *high protein, high vitamin diet*. We ask the patient to eat  $\frac{1}{2}$  to  $\frac{3}{4}$  pound of rare, red, ground meat per day, also  $\frac{1}{2}$  pound of liver three times per week, wheat germ and raw vegetables and raw fruit daily. The remainder of the diet is left to the discretion of the patient. It is advisable to have the meat ground, rather than advise new dentures as this is time-consuming and most patients would not sacrifice their remaining front teeth for an uncertain chance of recovery.

The diet is prescribed with the idea of overcoming the deficiency state, so that the synthetic preparations will not need to be administered indefinitely. We have treated cases without the diet for control purposes and can obtain complete relief

without it, but when the nicotinic acid and thiamin chloride are withdrawn, the attacks will recur.

Eleven of these patients have been observed for a period of six months without recurrence. The remaining nine have been placed on treatment during the past five months; the follow-up period is somewhat shorter, but of the twenty patients, seventeen remain entirely free from vertigo and the remaining three are markedly improved.

**Illustrative Cases.**—The following three cases are selected at random from the series:

**Case I.**—A white woman, aged thirty-six years, entered the Cleveland Clinic complaining of tinnitus in the left ear of fifteen years' duration, with associated impairment of hearing on

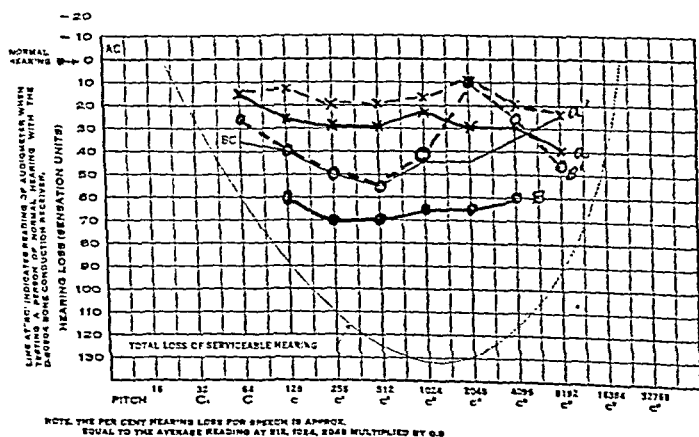


Fig. 75 (Case I).—*a*, Right ear before treatment; *a*<sup>1</sup>, right ear after one month of treatment; *b*, left ear before treatment; *b*<sup>1</sup>, left ear after one month of treatment.

the left. The right ear seemed perfectly normal. About three years previously she developed spells of rotational vertigo, lasting about one hour, accompanied by nausea and vomiting, and attacks would recur about once per month. This was followed by a remission of the vertigo for six months, but two months prior to entry she noted a recurrence. This time the

attacks were more severe and more frequent and would now occur two to three times a week and she would stagger to the left. The caloric test was hypo-active bilaterally. Audiogram revealed bilateral deafness more marked on the left.

The patient was placed on routine treatment, consisting of a high-protein, high-vitamin diet, nicotinic acid (250 mg. per day) and thiamin chloride (20 mg. per day) and returned in one month for recheck audiogram as shown in Fig. 75. Hearing improved as noted in the audiogram; the tinnitus was barely audible and she experienced three mild attacks of vertigo the first week after being placed on this treatment. There was no vertigo subsequently.

*Case II.*—A white man, aged fifty-seven years, came to the Cleveland Clinic complaining of attacks of rotational vertigo of six months' duration. About two months before ad-

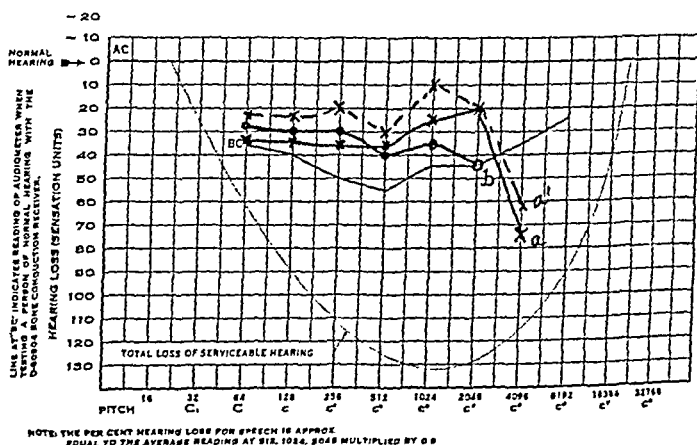


Fig. 76 (Case II).—*a*, Right ear before treatment; *a'*, right ear after two months of treatment; *b*, left ear, before and after treatment.

mission he noted loss of hearing on the left with constant tinnitus on left. Spells would occur almost daily and were not accompanied by nausea or vomiting. He would stagger to the right or left. There was a normal caloric response bilaterally.

The patient was placed on the routine treatment and audio-

grams before and two months after treatment are shown in Fig. 76. Hearing in the left ear remained unchanged. There was some improvement on the right, but not enough to exclude the possibility of error or the fluctuation in hearing accompanying this syndrome. He has been completely free of vertigo since one month after being placed on this treatment. The tinnitus is barely audible but is still present.

*Case III.*—A white man, aged fifty-two years, had a history of simultaneous onset of tinnitus in right ear and spells of rotational vertigo, beginning three years previously. The

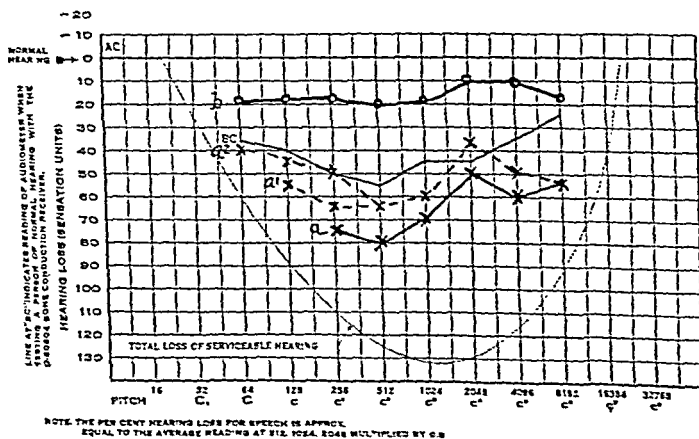


Fig. 77 (Case III).—*a*, Right ear before treatment; *a*<sup>1</sup>, right ear after two months of treatment; *a*<sup>2</sup>, right ear after three months of treatment; *b*, left ear before and after treatment.

vertigo subsided in about three months, but the tinnitus and deafness persisted in the right ear. The vertigo recurred six weeks before admission and was more severe, occurring two to three times daily. There was no associated nausea or vomiting. The caloric response was normal bilaterally. The induced vertigo was identical with his attacks. The patient was placed on routine treatment and returned two months later, at which time a recheck audiogram (Fig. 77) revealed improvement of hearing. There has been no vertigo since the

first week after treatment. The tinnitus is very mild but is still present. The patient returned a second time for recheck audiogram one month later, making a total of three months after beginning this treatment, and further improvement of hearing was noted, as shown in Fig. 77.

**Summary.**—The treatment with nicotinic acid and thiamin chloride should not be considered a cure for all cases of Ménière's syndrome. Not a large enough series of patients has been treated; nor has enough time elapsed to draw definite conclusions.

This form of therapy was used only in the idiopathic group of cases of Ménière's syndrome. Obviously we would not expect this form of treatment to benefit the patient who has a closed eustachian tube or the rare case of intralabyrinthine hemorrhage. However, our experience so far would indicate it is definitely beneficial in this selected group of cases.

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## SOME APPLICATIONS OF MEDICAL DIATHERMY

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MEDICAL diathermy is the production by high-frequency currents of heat in the body tissues for therapeutic purposes. This heat, however, is insufficient in amount to produce temperature high enough to destroy the tissues or impair their vitality.

It was first demonstrated in 1897 by D'Arsonval<sup>1</sup> that by passing a high-frequency current through the body tissues heat was produced in those tissues. This led to the development of the so-called "spark-gap" or the conventional diathermy machine. With the development of the radio, powerful oscillator tubes have been constructed for the production of high-frequency currents of short wave-length, which have today replaced many of the old spark-gap diathermy machines.

The value of medical diathermy has been extolled in many articles in the literature. In the following paragraphs is a brief description of some of the various uses of medical diathermy in clinical medicine.

### ARTHRITIS

In the treatment of arthritis, heat has its most extensive and varied application both systemically and locally. The common physical triad for treating arthritis is heat, massage, and therapeutic exercises. These measures serve to stimulate the defensive powers of the body through speeding up the general circulation, relieving pain, and overcoming swelling and stiffness of the affected joints. Short-wave diathermy has become recognized in recent years as an efficient form of deep heating. It is especially valuable for the larger areas, such as a shoulder, elbow, knee, or back. When it is applied over

an acute joint, it should be used for a short period and of low intensity for the first treatment, for at times medical diathermy in arthritis may cause an aggravation of the local symptoms. Best results are obtained if the treatment can be daily, especially if the patient is in the hospital. If it is impossible to give daily treatments, the patient should be instructed in the use of heat at home during the interval.

Permanent benefit or a cure should not be expected from the local treatments alone. The patient's general physical condition should be taken into consideration, and it is important to eliminate any foci of infection, especially specific infection, anemia, hypometabolism, obesity, or any other abnormal physiologic finding.

If it is remembered to use medical diathermy as an *ad-junct* rather than as a *cure* in arthritis, better and more rapid benefits will be derived from the physical agent.

#### BURSITIS

The value of diathermy in bursitis is sometimes questioned, especially when calcareous deposits are present. In many instances bursitis will repair itself without any type of treatment, provided sufficient time is given. It has also been observed that if the calcareous material is present at the first examination and if checked by roentgen ray at a later date the material is absorbed.

Diathermy is without question an aid to relieve pain, tenderness, and muscle spasm and for the promotion of the absorption of the calcareous deposits. Surgeons who have observed the results of diathermy in this condition are of the opinion that in many cases it eliminates the former routine of operating and cleaning out the bursa. During the acute inflammatory stage, diathermy should be avoided or should be used at low intensity. If the symptoms are aggravated, luminous heat or ice bags may be more beneficial. After the acute symptoms begin to subside, diathermy may be used at an increased intensity, followed by a corresponding increase in massage and by graduated exercises.

Feldman<sup>2</sup> studied 100 cases of subdeltoid bursitis with the entire group manifesting calcification of varying degrees verified by roentgen examination. All patients received short-wave diathermy, massage, manipulation, and reeducational exercises. Treatments were given daily for the first week, then every other day for the next week, then twice weekly for the next two or four weeks or until functional restoration had been achieved. Feldman's opinion after evaluating his results is that diathermy should be given a definite trial before extreme measures are instituted.

In 200 cases reported by Ferguson,<sup>3</sup> the treatment advocated was conservative except in the acute subdeltoid bursitis with calcification. In chronic bursitis, surgery should not be considered until the patient has had conservative treatment for at least one month.

#### FRACTURES

In the treatment of fractures today, it is felt that efficient physical therapy should be employed early. If this is done, much of the after-treatment of fractures can be avoided and better results obtained. If the injured part is treated with heat and the adjacent parts receive gentle stroking, circulation is improved and absorption of extravasated blood and relief of muscular spasm is hastened.

Murray<sup>4</sup> states that physical therapy helps to minimize the chances of delayed union and nonunion. It prevents the organization of scar tissue in muscle and soft parts about vessels and nerves, in joint capsules, and in tendons. When the bone is healed, functional limitation is reduced to a minimum. He suggests the use of heat, massage, and stimulation of muscles. The heat should always be moderate and not of high intensity, whether from a heating lamp or the diathermy machine.

The value of diathermy in nonunion of fractures is a debated question.

In experimental work with dogs, Weinberg and Ward<sup>5</sup> have demonstrated that diathermy elevates the temperature of the bones with an increase of local circulation, and that the

increased physiologic activity accelerates the formation of new bone. Because of the increased local circulation and nutrition, Cotton<sup>6</sup> is of the opinion that diathermy, baking, and massage are adjuncts of definite value in conjunction with other measures to build up the patient's general condition.

Voshell<sup>7</sup> analyzed 38 cases of nonunion in which diathermy was used. Favorable response occurred in 78.9 per cent. His opinion was that diathermy hastened organization of callus, so that nonunion is prevented or the length of the delay period is shortened. He advises the use of diathermy in all cases where development of the callus does not seem to be consistent with one's expectations.

#### SPRAINS AND MYOSITIS

In a sprain, injury may occur to the entire structure, many including bones, cartilage, joint capsule, ligaments, muscles, blood vessels, and supporting soft tissues. Kovacs<sup>8</sup> states that after a definite diagnosis severe sprains must be immobilized in molded and removable plaster splints. Besides the use of external forms of heating, the early use of diathermy has proved especially effective for the reduction of swelling and promotion of absorption. Graduated muscular contractions by low-frequency currents offer considerable additional help.

For the condition commonly called "tennis elbow," which frequently occurs after severe muscular exertion, Hansson and Horwich<sup>9</sup> suggest treatment by giving the forearm physiologic rest by means of a cock-up splint, diathermy followed by ten minutes of massage.

Tenosynovitis or inflammation of the tendon sheaths, when traumatic, usually yields promptly to the application of the short-wave current.

Acute myositis is characterized by an acute ache in the affected muscle, which is tender to pressure and held rigid in order to prevent movement. Local treatment in acute cases consists of the application of luminous heat or diathermy followed by massage.

In chronic cases the treatment is again heat, followed by

massage. Stretching exercises should be used with increasing intensity. General constitutional treatment should also be carried out.

### NEURITIS AND NEURALGIA

After a definite diagnosis of neuritis, the etiologic agent should be removed whenever demonstrable. General medical methods should be utilized with physical agents. Neuritis may occur in many different nerves in the body, but the principles of treatment are much the same. The response may vary greatly with the use of diathermy. In some instances complete and sudden relief may be obtained and in others no effect occurs, or diathermy may even intensify the symptoms. It is always well to begin with a small dose in the acute case, and if well tolerated the dosage can be increased in subsequent treatments.

Trifacial neuralgia is sometimes favorably influenced by diathermy. In some patients complete and permanent results are obtained, while in others no benefit is noted. These patients, however, should always be given the benefit of this form of therapy.

In Bell's palsy in the early stage of the disease, some form of heat should be applied to increase the circulation to the involved part, to reduce inflammation, and to speed up absorption of exudate. One may use either infra-red radiation or short-wave diathermy by the electromagnetic induction method, which secures a soothing deep heat. More recently we have used galvanic stimulation with the diathermy in the acute case, and we feel a more rapid recovery results.

We have not seen favorable response to diathermy in patients with intercostal neuritis or herpes zoster. However, diathermy should be used even if it relieves pain only temporarily.

### PNEUMONIA

The value of diathermy in pneumonia is still questioned by many clinicians. From various reports the usual clinical effects observed in an uncomplicated case of lobar pneumonia

are the relief of pain, relief of dyspnea and cyanosis, improvement of the heart action, general sedation and often an induction of sleep. The fact that medical diathermy is of benefit in reducing the severity of the thoracic pain makes it a valuable adjunct in the treatment of pneumonia.

Stewart<sup>10</sup> has used diathermy for treating pneumonia over a period of fifteen years and is of the opinion that it has proved of steadily increasing value as an adjunct in the treatment of this disease and definitely decreases the mortality rate. Coulter<sup>11</sup> in his observations found no evidence of a specific response in pneumonia to medical diathermy, but it did seem to be of definite benefit in reducing the severity of the thoracic pain.

Wetherbee, Foley, and Resnik<sup>12</sup> reported a series of 36 consecutive patients with lobar pneumonia who were given the standard treatment for this disease, including serum and oxygen when indicated. In addition one half of the patients, alternately chosen, were given medical diathermy. Their results indicated that diathermy greatly adds to the comfort of the patient and that it appears to lower the mortality.

The technic will vary some according to the patient's general condition, but best results are obtained if diathermy is given at low intensity two or three times daily. Applications are made on the chest and also to the back when possible from fifteen to sixty minutes.

Symptomatic improvement can be obtained in acute and chronic bronchitis. In acute cases there is usually relief from the pain and soreness in the chest; in chronic cases there is less cough and easier expectoration.

#### GASTRO-INTESTINAL TRACT

Because of the sedative effect of medical diathermy, we have used it, in addition to medical and dietary control, in the treatment of patients with severe irritable colon. The results have been satisfactory.

#### GENITO-URINARY TRACT

In acute and chronic hemorrhagic Bright's disease, Stone<sup>13</sup> states that diathermy given through the kidney regions may

be followed by beneficial results. The reports in the literature are very limited, and no definite conclusions can be made.

In four out of five of our patients with anuria following surgery, urinary flow was definitely started or markedly benefited by diathermy over the kidneys. The dose was of medium intensity and was given twice daily for about twenty minutes.

With the development of artificial fever, and more recently with the development of sulfanilamide and its derivatives, gonorrhea and its complications are being successfully treated by these methods. A certain number of these patients, however, cannot be treated in this way and therefore should have the aid of any physical agent that may be beneficial.

Harrison<sup>14</sup> believes that diathermy is the treatment of choice in those cases of acute prostatitis occurring either as a complication of an acute urethritis or in that smaller group of cases in which the infection is hematogenous from disease elsewhere, such as in influenza. In chronic prostatitis he states it is true that the symptoms are relieved, but in other respects the condition is similar to that in cases treated by digital massage; in other words, discouraging. In acute epididymitis, the elevation of temperature by diathermy is distinctly beneficial for the relief of pain and hastens the subsidence of the infection. If used in acute epididymitis, medical diathermy should be employed only as an adjunct to rest in bed with the testicles elevated, forcing of fluids, medication, and possibly nonspecific protein therapy.

#### GYNECOLOGY

In pelvic inflammatory diseases, the benefit that diathermy accomplishes is in all probability due to the hyperemia brought about by the local application of heat.

Coulter and Osborne<sup>15</sup> made a comparative study in pelvic heating, using diathermy machines with various wave-lengths, and the highest temperatures obtained were nearly 102° F., which were produced by electromagnetic field.

Horowitz and others<sup>16</sup> obtained similar results using the usual methods of application. In further experiments metal vaginal electrodes were used, and in 210 pelvic short-wave and

ultrashort-wave treatments the temperature varied between 100.6° and 111° F., averaging 107.5° F. At the same time rectal, cervical, and bladder temperatures were studied, which demonstrated that the cavity electrode is far superior to other electrode arrangements for the production of high local temperature elevations in the pelvis.

Waters<sup>17</sup> reported clinical results from medical diathermy obtained in 120 obstetric and gynecologic patients. In 64 patients with severe leukorrhea, endometritis, and myometritis, all but 4 made satisfactory recovery. In 8 cases of subinvolution of the uterus, 7 patients responded promptly to therapy. In 10 cases of dysmenorrhea, 4 patients failed to respond, though none showed gross pelvic abnormalities. In the 6 patients who had complete relief, the pain recurred in 4 at subsequent menstrual periods.

#### EYE

Diathermy has the same physiologic effect on the eye as it has on other tissues in the body, that is, vasodilatation with increased blood supply, followed by relief of pain in the congested types of infection. Ruedemann<sup>18</sup> and I believe diathermy is of definite value in deep-seated lesions of the globe and orbit, regardless of whether congestion is due to infection or some general inflammatory process. In the past year we treated various eye conditions in 60 patients. The results were favorable enough to warrant medical diathermy in the treatment of inflammatory conditions of the eye.

In an early report, Gifford<sup>19</sup> stated that the indications for medical diathermy in diseases of the eye are by no means well established, but in a more recent article, he expressed the opinion that local short-wave diathermy may prove to be of considerable clinical value in the treatment of chronic uveitis and of cellulitis of the lids and orbit.

#### SINUSITIS

Much controversy exists about the value of diathermy in the treatment of sinusitis. Various studies have been made

to determine if the temperature in sinuses or sinus mucosa is elevated by the use of short-wave diathermy. Another question to answer is whether or not the temperature in the sinuses must be elevated to be of value in treating sinusitis. Andreen and Osborne<sup>20</sup> made temperature studies when using various heating agents and found that the greatest temperature rise occurred in the mucosa lining the sinuses when long-wave diathermy and the electromagnetic field was used. Rosenwasser and Bierman<sup>21</sup> studied the effect of the short-wave current on the temperature of the paranasal sinuses and demonstrated that it was possible to elevate the temperature in the nose, in the antrums, and in the sphenoid sinuses by means of the short-wave current. The preceding application of a solution of cocaine and epinephrine interferes with this rise.

Leichner and Schmidt<sup>22</sup> treated 55 cases of sinusitis with ultrashort-wave diathermy. They used a combined treatment of first giving a nasal lavage with warm salt solution and then applying short-wave diathermy. Their impression was that diathermy presents a conservative method of treatment which not only eliminates infection from the sinus but improves the circulation and guards against reinfection. In 55 cases treated, 39 showed eminently satisfactory results.

Short-wave diathermy is most effective in the acute and subacute forms of nasal sinusitis according to Hollender.<sup>23</sup> Treatments should be given daily for from ten to fifteen minutes. Relief of pain is prompt. Drainage is improved, and in many instances the course of the disease is shortened. He points out that at no time should short-wave diathermy be employed to the exclusion of other indicated procedures. Its rôle is merely that of a therapeutic adjunct.

#### PYOGENIC INFECTIONS

Schliephake<sup>24</sup> reported the first short-wave treatment of humans when he treated himself for a nasal furuncle in March, 1929. The serious results from furuncles about the nose and upper lip are well known.

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The term most commonly applied to these diverticula is "pharyngo-esophageal diverticulum." It represents a herniation of the mucous membrane at the junction of the pharynx with the esophagus, where the muscle coats do not completely surround the tube. The opening may be small or large, and the pouch may reach such a size that it produces a tumor mass in the neck. When the pouch is filled with food, it compresses the esophagus from without, resulting in obstruction. The patient may learn certain manipulations by which he can empty the pouch.

The symptoms are usually present for several years before the physician is consulted. The patient locates the obstruction high in the esophagus, and there may be a return of food eaten a day or two previously. The patient frequently describes "a noise in the throat" on swallowing. Excessive secretion of mucus is often present, particularly during the night hours. Owing to the accumulation of food in the sac, there may be an unusually foul breath. Obstruction may be very mild, if present at all, during the early years of development. As the diverticulum slowly becomes larger, both solid and liquid foods become obstructed.

The diagnosis is made by roentgen examination, using a thin suspension of barium sulfate. However, if the roentgen findings do not completely explain the patient's symptoms, esophagoscopy examination is indicated. The danger of using bougies blindly is obvious. The treatment of pharyngo-esophageal diverticulum is surgical removal.

*Traction diverticula* are usually of academic interest only. In our experience, the patient has no symptoms attributable to their presence. They are the result of distortion of the esophagus by the pull of contracting scar tissue in some adjacent inflammatory process. They are tent-shaped with the base toward the esophageal lumen, and therefore empty readily and rarely cause dysphagia. Although they may be discovered during the course of a routine roentgen examination of the gastro-intestinal tract, they are usually an incidental finding at autopsy.

**Foreign Bodies.**—In these cases there is usually a history that the patient swallowed a foreign body. The degree of dysphagia varies from slight discomfort on swallowing to complete obstruction. In children there may be definite interference with respiration, in addition to difficulty in swallowing. If the dysphagia is marked, immediate esophagoscopy and removal are, of course, indicated. It is dangerous to attempt to push the foreign body into the stomach by bougies.

When the obstructive symptoms are mild, it is well to remember that a foreign body may remain in the esophagus for some time without causing complications. If the foreign body passes through the esophagus, there is usually little difficulty in its passage through the intestinal tract unless it is an unusually long object, provided the patient stays on his regular diet and bulky foods as well as cathartics are avoided.

If the foreign body is opaque to roentgenograms, its location is easily determined by the roentgen examination. If not opaque, the use of the barium meal may demonstrate a filling defect with a forked stream of the barium passing on each side of the foreign body. There may be a retention of the opaque medium in a pocket about the foreign body, or only a spasm or slight hesitation of the barium at this level may be observed fluoroscopically. On the other hand, the presence of the foreign body may be revealed by the adhesion of a small amount of barium to it when the remainder of the barium has reached the stomach. Foreign bodies are commonly found at the level of the clavicles.

The indications for esophagoscopy, examination and removal depend on many features, such as the size and shape of the foreign body, the amount of dysphagia present, and the roentgen findings.

**Carcinoma of the Esophagus.**—In our experience the most common cause of dysphagia in a patient past forty years of age, particularly if the patient is a man, is carcinoma of the esophagus. Carcinomas of the esophagus comprise about 7 per cent of all carcinomas found at autopsy.

*Incidence.*—In our series of cases, approximately 80 per

cent were in men, and the greatest number were in the fifth decade. Although the average age was fifty-nine years, the ages varied from thirty-eight to eighty-three years.

*Pathologically* the type of lesion is usually a squamous-cell carcinoma or transitional adenocarcinoma. However, many of the so-called cancers of the lower end of the esophagus are in reality extensions from carcinoma of the cardiac end of the stomach. Macroscopically, three types are found: the proliferative or cauliflower type, the ulcerative which has a hard edge, or the infiltrating or scirrhus type. As a rule metastases do not occur early.

*Location.*—In the male sex the most common location we found was in the middle and lower third of the esophagus, while in the female sex the upper third was the most common site. The growth commonly occurs at one of the constrictions of the esophagus.

*Symptoms.*—The most common early symptom found was difficulty in swallowing *solid* food, the point of obstruction depending on the site of the lesion. The patients may describe the difficulty in swallowing as a regurgitation of food they attempt to swallow. Other early symptoms include a burning sensation or discomfort behind the sternum, in the epigastrium, or between the scapulae. The onset of dysphagia will depend on whether the lesion is the stenosing or nonstenosing type and on the care the patient uses in the selection and mastication of his food. Sooner or later even liquids may be difficult to swallow. *Painful* swallowing is a *late* symptom if it is present at all. Unusual loss in weight is a prominent feature. The average duration of symptoms in our cases was *five months*.

*Diagnosis.*—We believe a provisional clinical diagnosis of carcinoma of the esophagus is justified when a patient in the carcinoma age, particularly if the patient is a man, presents a relatively short history of dysphagia without a history of trauma to the esophagus. If the lesion is extensive, the roentgen examination alone is sufficient to establish the diagnosis. However, if the roentgen findings are negative or are not ob-

viously diagnostic, esophagoscopy and possibly biopsy must be done. If the diagnosis is still not clear-cut, the patient must be observed at monthly intervals until the provisional diagnosis of carcinoma is proved or disproved.

Occasionally the symptoms are indeterminate, particularly in patients who do *not* have a stenosing lesion. Mathews and Schnabel<sup>3</sup> have recently reviewed 247 cases of carcinoma of the esophagus observed at the Philadelphia General Hospital, and of this number 108 came to autopsy. In 20 per cent of the 108 cases, the nonstenosing type of carcinoma was found. The most common symptoms were weakness, loss of weight, pains in the chest, vomiting, cough, and hoarseness. The clinical course was only one third as long as that of the stenosing variety.

*Prognosis.*—It is well known that the prognosis in carcinoma of the esophagus is not good. However, an early diagnosis may *prevent needless further examinations* and, if the symptoms are referred to the epigastrium, prevent possible exploration.

*Treatment.*—In view of the fact that metastases occur relatively late, resection of the esophagus has been done with encouraging results in instances where the diagnosis has been made early. However, usually by the time the physician sees the patient and the diagnosis is made, such a radical procedure seems to be rarely justified. Radium and roentgenotherapy have not materially affected either the morbidity of the disease or the duration of life. Since squamous-cell carcinoma of the skin and cervix uteri may be cured by the use of radium, it would seem logical to continue efforts with radium therapy. The element can be placed accurately by esophagoscopy or can be suspended on a small Levin tube, controlled by fluoroscopy.

Two palliative measures are commonly used, gastrostomy and dilatations. Dilatation from above, using graduated metal olive-type bougies passed on a previously swallowed silk string or graduated mercury-filled dilators, seems to be the procedure which has prolonged life in greatest comfort. I have seen patients live many months in comparative comfort while having

dilatations at bi-weekly or tri-weekly intervals. Carcinoma of the esophagus usually grows slowly.

**Benign Tumors of the Esophagus.**—In our experience benign tumors of the esophagus are pathologic curiosities. If any tumor is present, it is usually malignant. In the literature rare instances are reported where a benign polyp has been forced up into the mouth during regurgitation, and microscopic examination has established the diagnosis.

**Cardiospasm.**—The second most frequent cause of dysphagia, particularly if the patient is a woman, is cardiospasm. In our experience it is the most common cause of true dysphagia in women, but it is occasionally encountered in men. In many respects cardiospasm presents the opposite clinical picture from that of carcinoma. It is most frequently encountered in women in the third and fourth decades, instead of in men close to the age of sixty. The average duration of symptoms is in terms of years rather than in months, the average period in our experience being *seven years* before adequate investigation is made. The dysphagia usually pertains to cold fluids, rather than to solid foods.

A word should be said about the confusion in the literature relative to the terminology used in this condition. The term "cardiospasm" was first suggested by Mikulicz in 1888, and it is still the one most commonly used. Chevalier Jackson prefers the term "preentriculosis," since it implies a location proximal to the stomach and omits reference to etiology. Mosher uses the term "fibrosis of the terminal portion of the esophagus"; and Hurst, of England, has popularized the term "achalasia of the cardia," that is, failure of relaxation of the cardia.

**Etiology.**—The most important early work relative to the pathogenesis of this condition was done by Rake.<sup>4</sup> In 1925 he found degenerative changes in Auerbach's plexus at the lower end of the esophagus in eleven cases examined at autopsy. The degenerative changes resulted in more or less complete disappearance of the ganglion cells. Rake's work has since been confirmed by Camreon,<sup>5</sup> Mosher and McGregor,<sup>6</sup> and by

Beattie.<sup>7</sup> Hurst<sup>8</sup> believes that this apparently functional condition is really the result of organic disease of Auerbach's plexus, that achalasia of the cardia is in fact the only well-established example of a localized disease of the autonomic nervous system. Mosher believes "fibrosis of the terminal portion of the esophagus" is due to low-grade infection transferred from neighboring organs, particularly organs in the abdominal cavity.

*Symptoms.*—An analysis of the symptoms of cardiospasm shows that epigastric pain frequently antedates the dysphagia. The intensity of the dysphagia may vary considerably over years of time. At times food can be swallowed with a fair degree of comfort, while at other times the closure may be complete, particularly when cold liquids are taken. As dilatation of the esophagus gradually supervenes, there may be retrosternal fullness or interscapular pain, as well as marked regurgitation of undigested food, gaseous eructations, and loss of strength and weight.

The roentgen features are characteristic. In no other esophageal lesion do we find so great a dilatation of the esophagus as that commonly found in cardiospasm. If no retained food is in the esophagus, the roentgen examination, using the barium suspension, will show a *smooth contour* and a *V-shaped constriction* at its cardiac end.

However, even though the roentgen findings are characteristic of cardiospasm, carcinoma cannot be excluded positively by this examination. Esophagoscopy is definitely indicated in all obstructive lesions of the esophagus. If neoplasm can be excluded, the prognosis is excellent. One or more dilatations of the constricted area usually result in permanent cures.

A word of caution should be mentioned relative to the interpretation of chest films in the presence of cardiospasm. Cases have been reported where roentgen diagnoses of mediastinal tumors have been wrongly made owing to the presence of much food in a dilated esophagus.

*Spasm of the Esophagus.*—Spasm of the esophagus, other than cardiospasm, may be attributable to many causes.

It may be the result of ulceration or the presence of a foreign body; or it may occur without any demonstrable lesion in the esophagus. In our experience spasm of the esophagus may be associated with chronic cholecystitis. The history, clinical findings, and roentgen examinations will usually make the differentiation clear. If the spasm is otherwise unexplained, progress examinations or esophagosopic examinations are clearly indicated.

**Globus Hystericus.**—Although globus hystericus is frequently encountered in neurotic persons, particularly women, it is not a true dysphagia. The ordinary "lump in the throat" must not be confused with difficulty in the swallowing of food. Nervous persons who have this symptom can usually swallow any type of food without evidence of obstruction. There is no anemia or loss in weight. A motor neurosis or a spasm of the motor nerves in the throat and larynx causes the sensation of a "lump in the throat." Nothing abnormal is found by roentgen or esophagosopic examination. Previously this condition was thought to be associated with enlargement or varicosity of the lingual tonsil. The treatment is psychiatric, with correction of the causative factor. Sedatives may be necessary at the start of the treatment.

**Esophagitis.**—Esophagitis is frequently a secondary process to any stenosing lesion, often aggravated by the stasis of foods and secretions. However, *even in the absence of stenosis*, Vinson and Butt<sup>9</sup> believe esophagitis is the most common disease of the esophagus. In 3000 autopsies they found the incidence was 213 cases or 7 per cent. It is important to note that in only 10 per cent of these cases was there previous clinical evidence of its presence. The most common *symptoms* were substernal burning or pain, dysphagia, and hematemesis. Esophagitis may follow vomiting due to various causes, or it may complicate gastric intubation.

As a rule roentgen and esophagosopic examinations are contraindicated in the acute stage of esophagitis, and usually chronic esophagitis cannot be recognized roentgenologically. There may be a spasm of the lower third of the esophagus without dilatation above the involved area.

In every patient who presents unyielding gastric symptoms or in whom *chronic* esophagitis may be suspected, esophagoscopy, if not gastroscopic, examinations are indicated, regardless of negative roentgen findings.

The treatment usually involves the use of olive oil before meals, cool milk, atrophine or tincture of belladonna to tolerance, and the use of sedatives if the pain is severe. Later a bland, smooth diet and the intermittent use of belladonna should be continued.

Such infections as tuberculosis, syphilis, and blastomycosis rarely involve the esophagus, but when they do dysphagia is the most prominent symptom.

**Chronic Peptic Ulcer.**—Chronic peptic ulcer of the esophagus, most frequently at the lower end, has the usual anatomic characteristics of a chronic ulcer of the stomach or duodenum. In 1899 Fraenkel observed the presence of heterotopic mucous membrane in the esophagus of a patient who died of esophageal ulcer, and the same observations have been made by others. Acid gastric juice is secreted and its presence is analogous to the peptic ulcers occasionally found in Meckel's diverticula of the ileum.

Jackson, in 1929, reported having seen 21 active ulcers and the scars of 67 healed ulcers during 4000 esophagoscopy examinations. Friedenwald, Feldman, and Zinn have reported 13 cases which were demonstrated by roentgen examination.

The *symptoms* are retrosternal discomfort or pain during the ingestion of solid foods and occasionally a half hour or more after meals. Early in the course of the disease it may last only a few minutes and is relieved by alkalis; later the distress or pain is prolonged and is followed by regurgitation. The patient is afraid to eat. Pain may radiate to the back, and hematemesis may occur. Perforation and death have been reported.

The ulcer is usually single and situated on the posterior wall in the lower end of the esophagus. The most common roentgen manifestation is spasm only, but the presence of an ulcer crater may be demonstrated if unusual care is used. Esophagoscopy may be necessary to establish the diagnosis.

The treatment is the same as that used in peptic ulcer of the stomach and duodenum.

**Esophageal Varices.**—Esophageal varices occasionally are responsible for an otherwise unexplained hematemesis. The presence of cirrhosis of the liver is confirmatory evidence of the nature of the lesion. Dysphagia is rarely a prominent symptom in these instances.

In roentgen examination the varices are best demonstrated by using a thick barium mixture. They appear as semicircular defects interspersed with lacelike areas of increased density, the latter representing the medium in the crevices between the veins. However, in view of the fact that the varices may not be demonstrable by roentgenogram, esophagoscopic examination may be necessary to establish the diagnosis.

**Cicatricial Stricture.**—In cicatricial stricture of the esophagus, the dysphagia is usually progressive, and in at least 90 per cent of the cases there is a definite etiologic factor, such as the ingestion of lye. In the remaining 10 per cent of cases the dysphagia has usually been present a long time and may be intermittent. Stenosis following the swallowing of corrosive poisons usually involves the lower two thirds of the esophagus because of the prolonged reflex closure of the cardiac sphincter.

The roentgen findings are characterized by the smooth borders of the involved area. The amount of dilatation above the lesion will, of course, depend on the degree of stenosis and on the severity of the spasm associated with the lesion.

The treatment involves gradual dilatation if the obstruction is not complete. Gastrostomy is a life-saving procedure in instances where the obstruction is complete.

*Compression stenosis* is rare. Aneurysm or mediastinal tumors rarely produce dysphagia because of the elasticity of the esophagus.

**Dysphagia of Anemic Women.**—This condition, which is often called the "Plummer-Vinson syndrome," apparently is an achalasia or failure of relaxation of the pharyngo-esoph-

ageal sphincter at the upper end of the esophagus. Hurst believes this is due to a constantly associated atrophic glossitis and pharyngitis. The tongue becomes smooth and glossy, and the condition extends to the mucous membrane of the pharynx, which in turn gives rise to a neuromuscular imbalance.

The anemia may be severe, and it is always the hypochromic microcytic type. The hemoglobin may be 50 per cent or less, and in these cases the spleen may be palpable. Since the anemia is associated with achlorhydria, this condition is now considered to be a form of simple achlorhydric anemia.<sup>10</sup>

Roentgen and esophagoscopy examinations give negative findings. The administration of large doses of iron cures the condition. Formerly, when this condition was considered a form of hysteria, the passage of a stomach tube or esophageal dilator was used as a psychotherapeutic procedure in addition to the administration of large doses of iron. The iron therapy should have been given the sole credit for cure.

**Diaphragmatic Hernia.**—The *traumatic* varieties of diaphragmatic hernia which follow a severe crushing injury, such as an automobile accident or gunshot and stab wounds, are well known. The incidence of the *nontraumatic* variety is greater than the traumatic, and it is being recognized far more commonly than heretofore in adults. The true congenital forms usually result in symptoms soon after birth and may be of serious consequence. The hernias occur through any part of the diaphragm where there is deficient embryological fusion, the most common sites being the hiatus pleuroperitonealis, or foramen of Bochdalek, the dome of the diaphragm, the esophageal hiatus, or the foramen of Morgagni.

We are particularly interested in the nontraumatic forms which are encountered in adults. These are usually hiatus hernias. They are being recognized far more frequently than heretofore because clinicians have become hiatus-hernia conscious, and the roentgenologist, in addition to the usual fluoroscopic examination of the stomach in the vertical position, is examining patients in the horizontal, supine, and Trendelenburg positions. The significance of a hiatus hernia will of

course depend on its size, the number of organs involved, and the amount of constriction with consequent ulceration or obstruction. If *most of the stomach is above the diaphragm, cardiorespiratory symptoms* soon after eating will predominate, particularly if the patient is in a *reclining position*, while if *most of the stomach is below the diaphragm gastro-intestinal symptoms will predominate*. In most instances of hiatus hernia, only a small portion of the cardiac end of the stomach is involved and the herniation occurs intermittently, such as *when the patient is in a horizontal position* or when there is an *increase in intra-abdominal pressure from any cause*.

The tissues that surround the esophagus as it passes through the hiatus may be abnormally lax. Although there may be a congenital weakness, the greater frequency in elderly persons suggests that it is due mainly to *senile changes in the tissues*. The condition is most often found in *short, stocky persons* who have the high, transverse type of stomach.

When the extent of herniation is small and intermittent, *there may be no symptoms*. As it becomes larger, a feeling of pressure or a dull ache may be experienced in the epigastrium or behind the lower part of the sternum. This comes on immediately after swallowing, particularly after a heavy meal, and it may radiate through to the back. If more of the stomach is in the hernia, the attacks are more severe, and the pain radiates up through the left side of the thorax and to the interscapular area. These may be associated with typical *phrenic pain*, referred to the left shoulder and down the left arm, closely simulating angina pectoris. If the hernia is large, there will be pressure on the heart and left lung immediately after eating, and this gives rise to shortness of breath, palpitation, and tachycardia, particularly if the patient lies down after eating. Varying degrees of dysphagia accompany the more extensive hiatus hernias. Patients who have a *thoracic stomach* as a result of a short esophagus have symptoms similar to those described, except that *they do not have dysphagia*.

The possibility of a hiatus hernia should therefore be con-

sidered when upper abdominal symptoms of doubtful origin occur *chiefly or only at night, or are associated with slight dysphagia or anginoid symptoms*. The symptoms are usually relieved by *sitting up, getting up and walking around*, by eructation after the ingestion of sodium bicarbonate or by vomiting. The pain may simulate gallstone colic, and intermittent dysphagia may be a prominent symptom. If there is no dysphagia, the possibility of thoracic stomach should also be considered.

If the hernial sac becomes incarcerated or constricted, the resulting congestion, venous stasis, inflammation, or ulceration may give rise to hematemesis or occult blood in the stools.

*Diagnosis.*—The diagnosis is made by the roentgen examination, the most important features of which are: (1) to *determine the length of the esophagus* and (2), to examine the patient in the *horizontal or Trendelenburg position*. A close study of the *mucosal markings* clearly differentiates between the fundus of the stomach and the *parallel longitudinal folds of the cardiac sphincter*. A procedure which will result in the maximum herniation is the following: During the fluoroscopic examination with the patient in the supine or Trendelenburg position, have him take a deep breath, hold it, and bear down. This increases the intra-abdominal pressure to the maximum. Films may be made during this procedure.

*Treatment.*—The treatment will, of course, depend upon many features. First, if the patient has a thoracic stomach as shown by the roentgen demonstration of a short esophagus, the treatment is obviously a medical problem. Second, if the treatment is of hiatus hernia, it will depend upon the size, upon whether or not it is incarcerated or fixed in position, and upon the severity of the symptoms.

The patient should avoid taking large meals at any one time and remain in the upright position for two or three hours after eating. Anything which tends to bring on the attacks should be avoided. In order to prevent nocturnal attacks, it may be necessary to raise the head of the patient's bed as far as possible. The attacks themselves can generally be stopped

by assuming the upright position and taking an effervescent drink. A smooth diet is definitely indicated, and if ulceration is present, the usual treatment for peptic ulcer is in order. Intestinal flatulence or anything which tends to increase intra-abdominal pressure should be reduced to the minimum.

If operation is necessary, Harrington prefers the intra-abdominal approach; although if the hernia is large, the use of the intrathoracic approach may be necessary. If organs other than the stomach are involved in the hernia, operation should be performed as soon as the diagnosis is made. Palliative interruptions of the phrenic nerve should be considered in selected cases in which reparative operation is contraindicated.

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ermy in pyogenic infections in all parts of the body. The course of the disease varied according to the stage at which the patient came for treatment. In the early stages, resolution was obtained in the majority of cases; in many it produced sharp demarcation and spontaneous drainage without surgical intervention. Usually the discharge ceased early, followed by a remarkably speedy healing. In those cases requiring surgical intervention, the ultrashort-wave therapy so effectively localized the lesion that the surgeon was permitted to operate at an earlier time with distinctly less surgical hazard.

### SUMMARY

Some of the common conditions in which medical diathermy may be of value are discussed, including: arthritis, bursitis, fractures, sprains, myositis, neuritis and neuralgia, pneumonia, sinusitis, pyogenic infections and conditions of the gastro-intestinal tract, the genito-urinary tract, the eye, and gynecologic and obstetric conditions.

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## DYSPHAGIA: CAUSES, DIFFERENTIAL DIAGNOSIS AND TREATMENT

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ALTHOUGH the incidence of dysphagia in general practice is relatively low, accurate differential diagnosis is important because much can be done for the patient who does not have a neoplasm. In this discussion the practical clinical features will be considered first, and this will be followed by a consideration of the roentgen features. The *diagnostic triad* involves (1), the accurate interpretation of symptoms, particularly as they relate to the type and duration of the dysphagia; (2), the roentgen findings; and (3), the esophagosopic findings. It is assumed that the routine physical examination and usual laboratory studies have revealed no significant findings pertaining to other parts of the body which may be causing reflex symptoms in the esophagus.

**Congenital abnormalities** encountered in the newborn infant often cause complete obstruction or are associated with a fistulous opening into the trachea or bronchi. Starvation or aspiration pneumonia is the cause of death in these instances. Other congenital narrowings of the esophagus may produce no symptoms for years. A congenital web (a fold of mucous membrane which extends across the lumen) may be present. These conditions can be treated through the esophagoscope.<sup>1</sup>

**Diverticula of the Esophagus.**—Of the two types, pulsion and traction diverticula, the pulsion or pressure type which is usually situated at the upper end of the esophagus is the only one of clinical significance. In rare instances this type of diverticulum may be situated in the lower end of the esophagus and may be the cause of respiratory symptoms.<sup>2</sup>